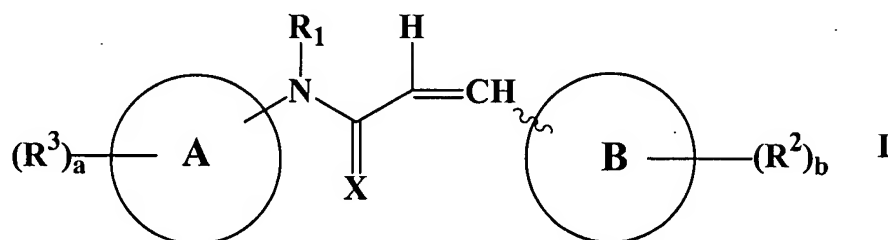


Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A compound of formula I:



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl, provided that ring A is other than pyridyl, quinazolyl or naphthyridyl;

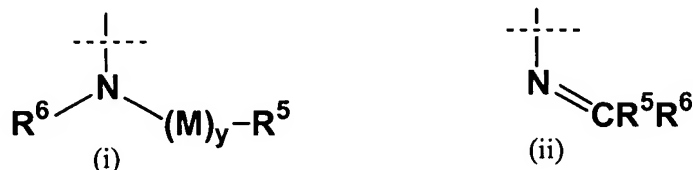
X is O or S;

R¹ is independently selected from the group consisting of -R⁴, -SO₂(C₁-C₆)alkyl, -C(=O)R⁴, -C(=O)OR⁴, -C(=O)O(C₁-C₆)alkylenearyl, -OR⁴, -(C₂-C₆)alkynyl, -(C₃-C₆)heteroalkenyl, -(C₂-C₆)alkylene-OR⁴, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C₁-C₃)alkyl, unsubstituted aryl(C₁-C₃)alkyl, substituted heteroaryl(C₁-C₃)alkyl and unsubstituted heteroaryl(C₁-C₃)alkyl;

each R² is independently selected from -OR⁴, halogen, -C≡N, -CO₂R⁴, -C(=O)NR⁴₂, -C(=NR⁴)NR⁴₂, -O(C₁-C₃)alkylene-CO₂R⁴, -(C₂-C₆)alkylene-OR⁴, phosphonato, -NR⁴₂, -NHC(=O)(C₁-C₆)alkyl, sulfamyl, carbamyl, -OC(=O)(C₁-C₃)alkyl, -O(C₂-C₆)alkylene-N((C₁-C₆)alkyl)₂, -S(C₁-C₃)alkyl, -S(=O)(C₁-C₃)alkyl, and -SO₂(C₁-C₃)alkyl;

b is 2, 3, 4, or 5;

R^3 is independently selected from halogen, $-(C_1-C_6)alkyl$, $-OR^4$, $-C\equiv N$, $-C(=NR^4)NR^4_2$, $-O(C_1-C_3)alkylene-CO_2R^4$, $-(C_1-C_6)alkylene-OR^4$, nitro, phosphonato, $-NHC(=O)(C_1-C_6)alkyl$, sulfamyl, $-OC(=O)(C_1-C_3)alkyl$, $-O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)_2$ and (i) and (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of $-(C_1-C_6)alkylene-$, $-(CH_2)_d-V-(CH_2)_e-$, $-(CH_2)_f-W-(CH_2)_g-$ and $-Z-$;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, $-C(=O)-$, $-C(=O)(C_1-C_6)perfluoroalkylene-$, $-C(=O)-$, $-C(=S)-$, $-S(=O)-$, $-SO_2-$, $-C(=O)NR^4-$, $-C(=S)NR^4-$ and $-SO_2NR^4-$;

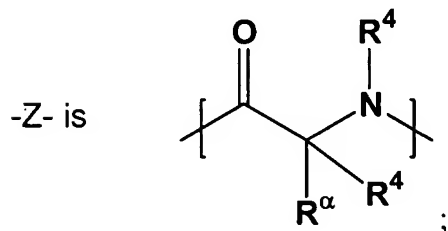
each W is independently selected from the group consisting of $-NR^4-$, $-O-$ and $-S-$;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of $-Z-$ is S or R, or a mixture of S and R;

each R^a is independently selected from the group consisting of $-H$, $-(C_1-C_6)alkyl$, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$,

-(CH₂)₂COOH, -CH₂-(2-imidazolyl), -(CH₂)₄-NH₂, -(CH₂)₂-S-CH₃, phenyl, -CH₂-phenyl, -CH₂-OH, -CH(OH)-CH₃, -CH₂-(3-indolyl), -CH₂-(4-hydroxyphenyl); and includes compounds wherein R^a and R⁴ combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R⁴ is independently selected from the group consisting of -H, -(C₁-C₆)alkyl, substituted -(C₁-C₆)alkyl, -(C₂-C₆)alkenyl, substituted -(C₂-C₆)alkenyl and heteroalkyl, wherein two R⁴ groups may together form a heterocycle;

each R⁵ is independently selected from the group consisting of -R⁴, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO₂R⁴, -C(=O)NR⁴₂, -C(=NH)-NR⁴₂, -(C₁-C₆)perfluoroalkyl, -CF₂Cl, -P(=O)(OR⁴)₂, -OP(=O)(OR⁴)₂, -CR⁴R⁷R⁸ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R⁵ is -CO₂R⁴, then R⁴ is not -H;

each R⁶ is independently selected from the group consisting of -H, -(C₁-C₆)alkyl, and aryl(C₁-C₃)alkyl,

each R⁷ is independently selected from the group consisting of -H, -(C₁-C₆)alkyl, -C(=O)R⁸, -OR⁴, -SR⁴, -OC(=O)(CH₂)₂CO₂R⁶, guanidino, NR⁴₂, -NR⁴₃⁺, -N⁺(CH₂CH₂OR⁵)₃, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R⁸ is independently selected from the group consisting of R^a, halogen, -NR⁴₂ and heterocycles containing two nitrogen atoms;

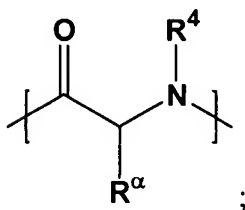
wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within [[Ar,]] R¹, R⁵ [[R⁶,]] and R⁷ ~~and~~ R^a are independently selected from the group consisting of halogen, -(C₁-C₆)alkyl, -(C₁-C₆)alkoxy, -NO₂, -C≡N, -C(=O)O(C₁-C₃)alkyl, -OR⁴, -(C₂-C₆)alkylene-OR⁴, phosphonato, -NR⁴₂, -NHC(=O)(C₁-C₆)alkyl, sulfamyl, carbamyl, -OC(=O)(C₁-C₃)alkyl, -O(C₂-C₆)alkylene-N((C₁-C₆)alkyl)₂ and -(C₁-C₃)perfluoroalkyl;

~~~~ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

provided that:

when A is phenyl,  $R^3$  is other than 3,4,5-tri-OR<sup>4</sup>;  
 when  $R^2$  is 4-methoxy,  $R^3$  is other than 4-methoxy;  
 when B is phenyl,  $R^2$  is other than 2,3-di-OR<sup>4</sup> and 3,4-di-OR<sup>4</sup>; and  
 when  $R^3$  is halogen,  $R^2$  is not chlorine, bromine or iodine;  
 or a salt of such a compound.

2. (currently amended) A compound according to claim 1,  
 wherein -Z- is:



wherein the absolute stereochemistry of -Z- is either S or R; and

each  $R^\alpha$  is independently selected from the group consisting of -H, -CH<sub>3</sub>, -(CH<sub>2</sub>)<sub>3</sub>-NH-C(NH<sub>2</sub>)(=NH), -CH<sub>2</sub>C(=O)NH<sub>2</sub>, -CH<sub>2</sub>COOH, -CH<sub>2</sub>SH, -(CH<sub>2</sub>)<sub>2</sub>C(=O)-NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>2</sub>COOH, -CH<sub>2</sub>-(2-imidazolyl), -CH(CH<sub>3</sub>)-CH<sub>2</sub>CH<sub>3</sub>, -CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, -(CH<sub>2</sub>)<sub>4</sub>-NH<sub>2</sub>, -(CH<sub>2</sub>)<sub>2</sub>-S-CH<sub>3</sub>, phenyl, CH<sub>2</sub>-phenyl, -CH<sub>2</sub>-OH, -CH(OH)-CH<sub>3</sub>, -CH<sub>2</sub>-(3-indolyl), -CH<sub>2</sub>-(4-hydroxyphenyl), -CH(CH<sub>3</sub>)<sub>2</sub> and -CH<sub>2</sub>CH<sub>3</sub>; and includes compounds wherein  $R^\alpha$  and  $R^4$  combine to form a 5-, 6- or 7-membered heterocyclic ring;

each V is independently selected from the group consisting of -C(=O)-, -C(=S)-, -S(=O)-, -SO<sub>2</sub>-, -C(=O)NR<sup>4</sup>-, -C(=S)NR<sup>4</sup>- and -SO<sub>2</sub>NR<sup>4</sup>-;

$R^2$  is independently selected from -OR<sup>4</sup>, -C≡N, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)NR<sup>4</sup>, -C(=NR<sup>4</sup>)NR<sup>4</sup>, -O(C<sub>1</sub>-C<sub>3</sub>)alkylene-CO<sub>2</sub>R<sup>4</sup>, -(C<sub>2</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, phosphonato, -NR<sup>4</sup>, -NHC(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl, sulfamyl, carbamyl, -OC(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, -O(C<sub>2</sub>-C<sub>6</sub>)alkylene-N((C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub>, -S(C<sub>1</sub>-C<sub>3</sub>)alkyl, -S(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>)alkyl;

b is 2 or 3;

each  $R^5$  is independently selected from the group consisting of  $-R^4$ , unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic,  $-\text{CO}_2R^4$ ,  $-\text{C}(=\text{O})\text{NR}^4_2$ ,  $-\text{C}(=\text{NH})-\text{NR}^4_2$ , and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and  $R^5$  is  $-\text{CO}_2R^4$ , then  $R^4$  is not  $-\text{H}$ ; and

each  $R^7$  is independently selected from the group consisting of  $-\text{H}$ ,  $-(\text{C}_1-\text{C}_6)\text{alkyl}$  and  $-(\text{C}_1-\text{C}_6)\text{acyl}$ ;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within  $[[\text{Ar}]]$ ,  $R^1[[,]]$  and  $R^5$  and  $R^6$  are independently selected from the group consisting of halogen,  $-(\text{C}_1-\text{C}_6)\text{alkyl}$ ,  $-(\text{C}_1-\text{C}_6)\text{alkoxy}$ ,  $-\text{NO}_2$ ,  $-\text{C}\equiv\text{N}$ ,  $-\text{C}(=\text{O})\text{O}(\text{C}_1-\text{C}_3)\text{alkyl}$ ,  $-\text{OR}^4$ ,  $-(\text{C}_2-\text{C}_6)\text{alkylene}-\text{OR}^4$ , phosphonato,  $-\text{NR}^4_2$ ,  $-\text{NHC}(=\text{O})(\text{C}_1-\text{C}_6)\text{alkyl}$ , sulfamyl, carbamyl,  $-\text{OC}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$ ,  $-\text{O}(\text{C}_2-\text{C}_6)\text{alkylene}-\text{N}((\text{C}_1-\text{C}_6)\text{alkyl})_2$  and  $-(\text{C}_1-\text{C}_3)\text{perfluoroalkyl}$ ; or a salt of such a compound.

3-7. (cancelled)

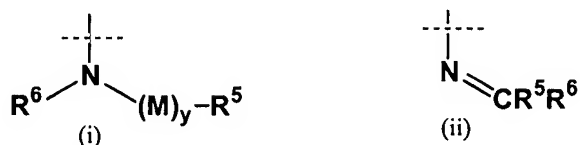
8. (currently amended) A compound according to claim 2 90, wherein:

one  $R^3$  substituent, designated  $R^{3p}$ , is positioned in a substitution orientation relative to the  $-\text{N}(\text{R}^1)-\text{C}(=\text{X})-\text{CH}=\text{CH}-\textcircled{\text{B}}-\text{R}^2$  moiety of Formula I which is closest to the planar angle formed by a para substituent in a six-membered aromatic ring and forms a planar angle with the  $-\text{N}(\text{R}^1)-\text{C}(=\text{X})-\text{CH}=\text{CH}-\textcircled{\text{B}}-\text{R}^2$  moiety of between about  $135^\circ$  and about  $180^\circ$ ; and

at least one  $R^3$  substituent, designated  $R^{3m}$  is positioned in a substitution orientation relative to the  $-\text{N}(\text{R}^1)-\text{C}(=\text{X})-\text{CH}=\text{CH}-\textcircled{\text{B}}-\text{R}^2$  moiety of Formula I which is closest to the planar angle formed by a meta substituent in a 6-membered aromatic ring and forms a planar angle with the  $-\text{N}(\text{R}^1)-\text{C}(=\text{X})-\text{CH}=\text{CH}-\textcircled{\text{B}}-\text{R}^2$  moiety of between about  $90^\circ$  and about  $145^\circ$ ;

wherein:

each  $R^{3m}$  is selected from the group consisting of nitro and (i) and (ii) below:



$R^{3p}$  is selected from the group consisting of halogen,  $-(C_1-C_6)\text{alkyl}$ ,  $-(C_1-C_6)\text{alkoxy}$ ,  $-C\equiv N$ ,  $-C(=O)NR^4_2$ ,  $-C(=NR^4)NR^4_2$ ,  $-O(C_1-C_3)\text{alkylene}-CO_2R^4$ ,  $-OR^4$ ,  $-(C_2-C_6)\text{alkylene}-OR^4$ , phosphonato,  $-NR^4_2$ ,  $-NHC(=O)(C_1-C_6)\text{alkyl}$ , sulfamyl,  $-OC(=O)(C_1-C_3)\text{alkyl}$ ,  $-O(C_2-C_6)\text{alkylene}-N((C_1-C_6)\text{alkyl})_2$  and  $-(C_1-C_3)\text{perfluoroalkyl}$ ;

wherein ring A, ring B, X, M, d, e, f, g, V, W, Z,  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ , a, b, y,  $R^a$ ,  $\sim$  and any remaining  $R^3$  substituents are as defined in claim 2 90; or a salt of such a compound.

9-10. (cancelled)

11. (withdrawn) A compound according to Claim 8 wherein:

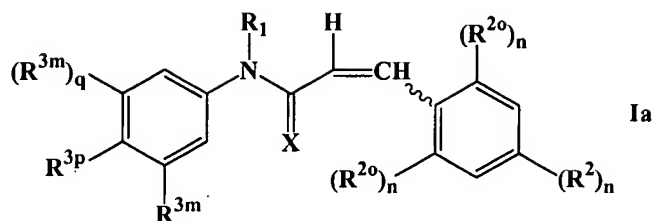
ring A is phenyl;

ring B is phenyl;

at least one  $R^2$  substituent, designated  $R^{2o}$  is positioned at an ortho- or 1,2-substitution orientation on ring B relative to the  $\sim CH=CH-C(=X)-N(R^1)-\textcircled{A}-(R^3)_a$  moiety of formula I; and X, M, d, e, f, g, V, W, Z,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^{3m}$ ,  $R^{3p}$ ,  $R^4$ ,  $R^5$ ,  $R^6$ ,  $R^7$ , a, b, y,  $\sim$  and  $R^a$  are as defined in claim 8; or a salt of such a compound.

12-14. (cancelled)

15. (withdrawn) A compound according to claim 11 of formula Ia:



wherein:

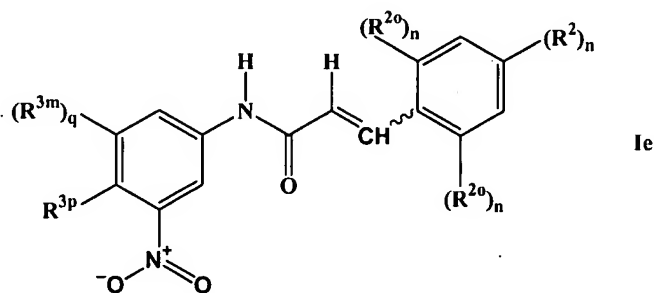
q is 0 or 1

each n is independently selected from 0 and 1; with the proviso that the sum of the values of n is selected from 2 and 3; and

~~~~, X, R<sup>1</sup>, R<sup>2</sup>, R<sup>2o</sup>, R<sup>3m</sup>, R<sup>3p</sup>, and n are as defined in claim 11;

or a salt of such a compound.

16. (withdrawn) A compound according to claim 15 of formula Ia



wherein:

q, n, R², R^{2o}, R^{3m} and R^{3p} are defined as in claim 15;

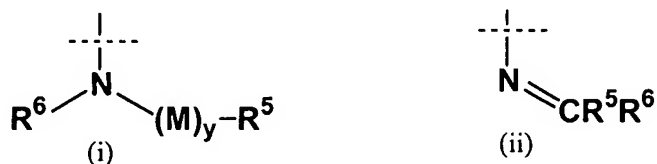
or a salt of such a compound.

17. (cancelled)

18. (withdrawn, currently amended) A compound according to claim 15

wherein:

each R^{3m} is independently selected from the group consisting of (i) and (ii) below:



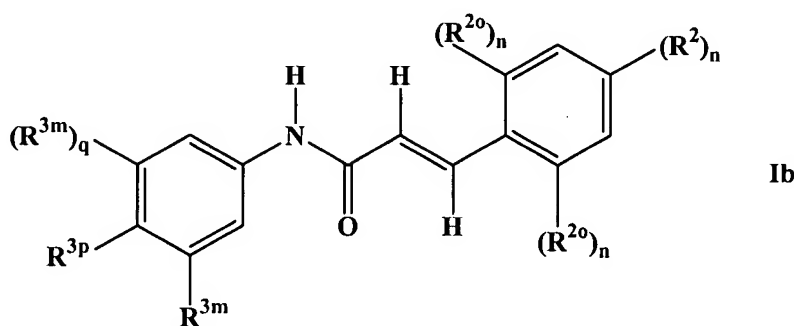
R^{3p} is selected from the group consisting of halogen, $-(C_1-C_6)\text{alkyl}$, $-(C_1-C_6)\text{alkoxy}$, $-C\equiv N$, $-C(=O)NR^4_2$, $-C(=NR^4)NR^4_2$, $-O(C_1-C_3)\text{alkylene}-CO_2R^4$, $-OR^4$, $-(C_2-C_6)\text{alkylene}-OR^4$, phosphonato, $-NR^4_2$, $-NHC(=O)(C_1-C_6)\text{alkyl}$, sulfamyl, $-OC(=O)(C_1-C_3)\text{alkyl}$, $-O(C_2-C_6)\text{alkylene}-N((C_1-C_6)\text{alkyl})_2$ and $-(C_1-C_3)\text{perfluoroalkyl}$;

each R^{2o} is independently selected from the group consisting of $-(C_1-C_6)\text{alkoxy}$, $-NR^4_2$, $-OC(=O)(C_1-C_3)\text{alkyl}$ and $-O(C_2-C_6)\text{alkylene}-N((C_1-C_6)\text{alkyl})_2$;

R^2 is selected from the group consisting of halogen, $-(C_1-C_6)\text{alkyl}$, $-(C_1-C_6)\text{alkoxy}$, $-NR^4_2$, $-C\equiv N$, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NR^4)NR^4_2$, and $-(C_1-C_3)\text{perfluoroalkyl}$; and

X, M, d, e, f, g, V, W, Z, R^1 , R^3 , R^4 , R^5 , R^6 , R^7 , a, b, n, y and R^a are as defined in claim 15; or a salt of such a compound.

19. (withdrawn) A compound according to claim 18 of formula Ib



wherein:

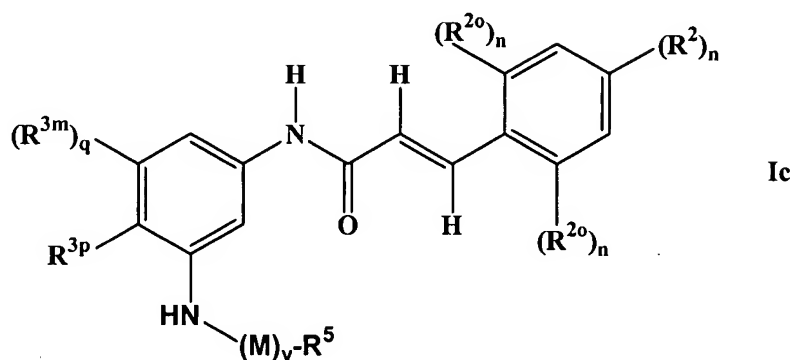
R^{2o} is $-(C_1-C_6)\text{alkoxy}$;

R^2 is selected from the group consisting of halogen, $-(C_1-C_6)\text{alkyl}$, $-(C_1-C_6)\text{alkoxy}$ and $-NR^4_2$;

q is 0 or 1; and
the conformation of the olefin double bond is *E*;
n, R^{3m} and R^{3p} are defined as in claim 18;
or a salt of such a compound.

20. (cancelled)

21. (withdrawn) A compound according to claim 19 of the formula Ic:



wherein R², R^{2o}, R^{3m}, R^{3p}, q, n, M, y and R⁵ are as defined in claim 19;
or a salt of such a compound.

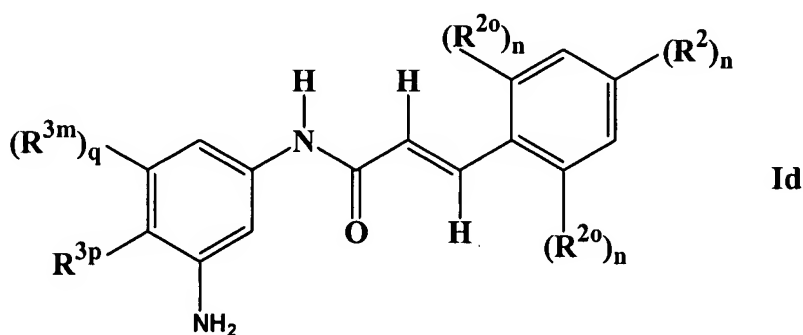
22. (previously presented) A compound according to claim 1, wherein the compound is selected from the group consisting of: (*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3,4,5-trimethoxyphenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,3,4,5,6-pentafluorophenyl)-2-propenamide; (*E*)-*N*-(4-bromophenyl)-3-(3-methoxy-4-fluorophenyl)-2-propenamide; (*E*)-*N*-(4-bromophenyl)-3-(3-cyano-4-fluorophenyl)-2-propenamide; (*E*)-*N*-(4-bromophenyl)-3-(3-carboxy-4-fluorophenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(3-fluoro-4-nitrophenyl)-2-propenamide; (*E*)-*N*-(4-bromophenyl)-3-(2,4-difluorophenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(3-fluoro-4-aminophenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-

phenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide; (*E*)-*N*-(4-methoxyphenyl)-3-(2,6-dimethoxyphenyl)-2-propenamide; (*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-3-nitrophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide; (*E*)-*N*-(4-methoxy-3-aminophenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide; 2-[(5-[(2*E*)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl)amino)sulfonyl]-acetic acid; 2-(*N*-{5-[(2*E*)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}carbamoyl)acetic acid; (2*E*)-*N*-[3-(amidinoamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; 2-({5-[(2*E*)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}amino)acetic acid; (2*E*)-*N*-{3-[(3,5-dinitrophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-{3-[(3,5-diaminophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[3-(2-chloroacetyl-amino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-{4-methoxy-3-[2-(4-methylpiperazinyl)acetyl-amino]-phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[4-methoxy-3-(phenylcarbonylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-{4-methoxy-3-[(4-nitrophenyl)carbonylamino]phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-{3-[(4-aminophenyl)carbonylamino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-{3-[(1*Z*)-1-aza-2-(4-nitrophenyl)vinyl]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[3-((2*R*)-2,6-diaminohexanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[3-((2*R*)-2-amino-3-hydroxypropanoylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[3-((2*S*)-2-amino-3-hydroxypropanoylamino)-4-methoxy-phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[3-(aminocarbonylamino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-[4-methoxy-3-(methylamino)phenyl]-3-(2,4,6-trimethoxy-phenyl)prop-2-enamide; (2*E*)-*N*-[3-(acetyl-amino)-4-methoxyphenyl]-3-(2,4,6-trimethoxy-phenyl)prop-2-enamide; (2*E*)-*N*-(3-{[(2,4-dinitrophenyl)sulfonyl]amino}-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-(3-{[(2,4-diaminophenyl)sulfonyl]amino}-4-methoxy-phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2*E*)-*N*-{3-[2-(dimethylamino)acetyl-amino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; 2-

({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} amino)propanoic acid; (2E)-N-(4-methoxy-3-{[4-(4-methylpiperazinyl)phenyl]-carbonyl-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-[3-(2-hydroxyacetyl-amino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-[4-methoxy-3-(2-pyridylacetyl-amino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)methyl acetate; (2E)-N-[3-(2-hydroxypropanoyl-amino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-{4-methoxy-3-[2-(triethylammonium)acetyl-amino]-phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-(4-methoxy-3-{2-[tris(2-hydroxyethyl)ammonium]-acetyl-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-[3-(2-hydroxy-2-methylpropanoyl-amino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; 1-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)-isopropyl acetate; (2E)-N-[4-methoxy-3-(2,2,2-trifluoroacetyl-amino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-(4-methoxy-3-{[(trifluoromethyl)sulfonyl]-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; 3-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}-carbamoyl)propanoic acid; 3-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)propanoyl chloride; 3-[(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)methyl]oxycarbonyl]propanoic acid; 4-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)butanoic acid; (2E)-N-{4-methoxy-3-[2-(phosphonoxy)acetyl-amino]phenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide, disodium salt; 4-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} amino)butanoic acid; 3-({5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} amino)propanoic acid; (2E)-N-[4-methoxy-3-(methoxycarbonylamino)phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (2E)-N-(4-methoxy-3-{[(4-methoxyphenyl)sulfonyl]-amino}phenyl)-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; (N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)ethyl acetate; methyl 3-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)propanoate; ethyl 2-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoyl-

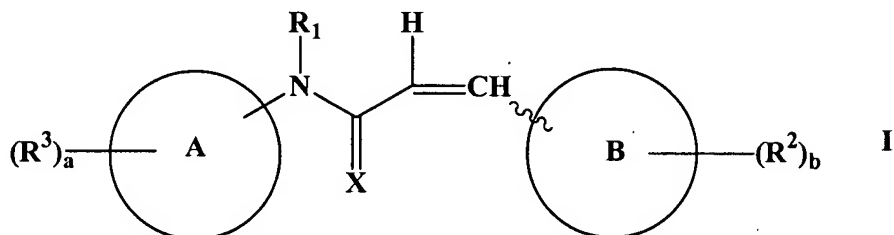
amino]-2-methoxyphenyl} carbamoyl)acetate; (2E)-N-[4-methoxy-3-(2,2,3,3,3-pentafluoropropanoylamino)-phenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; methyl 2-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoyl-amino]-2-methoxyphenyl} carbamoyl)-2,2-difluoroacetate; 3-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl}-carbamoyl)-2,2,3,3-tetrafluoropropanoic acid; (2E)-N-[3-(2-aminoacetyl-amino)-4-methoxyphenyl]-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; 2-(N-{5-[(2E)-3-(2,4,6-trimethoxyphenyl)prop-2-enoylamino]-2-methoxyphenyl} carbamoyl)-2,2-difluoroacetic acid; (2E)-N-{3-[2-(dimethylamino)-2,2-difluoroacetyl-amino]-4-methoxyphenyl}-3-(2,4,6-trimethoxyphenyl)prop-2-enamide; and salts of such compounds.

23. (withdrawn) A compound according to claim 21 of the formula Id:



wherein R^2 , R^{2o} , R^{3m} , R^{3p} , n , and q are defined as in claim 21, or a salt of such a compound.

24. (previously presented) A process for preparing a compound according to claim 2, which compound has the formula I,



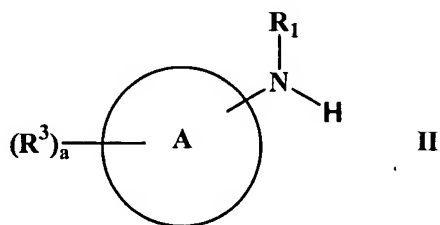
wherein:

the olefin double bond is in the *E* conformation; and

R^1 , R^2 , R^3 , a , b , X , A and B are as defined in claim 2;

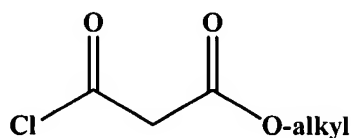
comprising:

(1) coupling a compound of formula II:

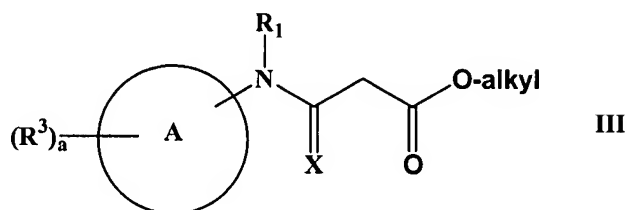


wherein A , R^1 , R^3 , and a are defined as in claim 2;

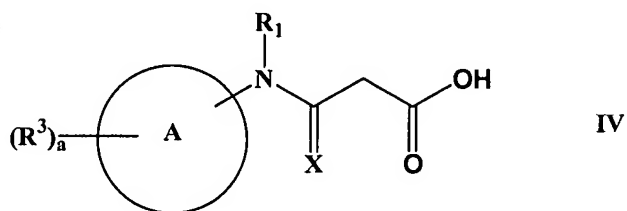
with an alkyl ester of malonic acid chloride:



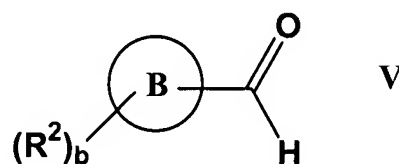
to yield a carboxylic ester compound of formula III:



(2) hydrolyzing the carboxylic ester compound of formula III to form a carboxylic acid compound of formula IV:

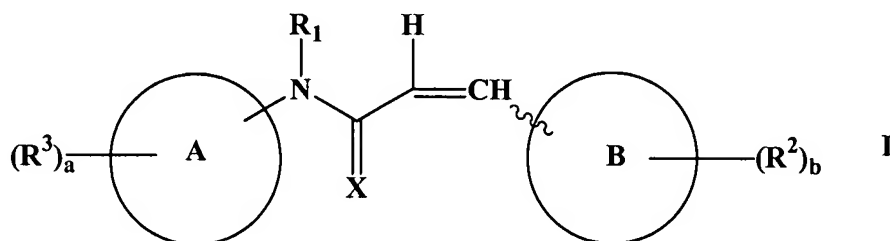


(3) coupling of the carboxylic acid compound of formula IV with an aromatic aldehyde of formula V:



wherein R^2 , B and b are defined as in claim 2;
in glacial acetic acid at elevated temperature to form a compound of formula I;
or a salt of such a compound.

25. (previously presented) A process for preparing a compound according to claim 2, which compound has the formula I,

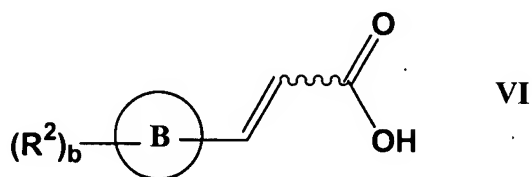


wherein:

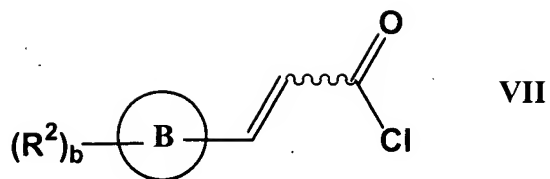
R^1 , R^2 , R^3 , a, b, X, A and B are as defined in claim 2;

comprising:

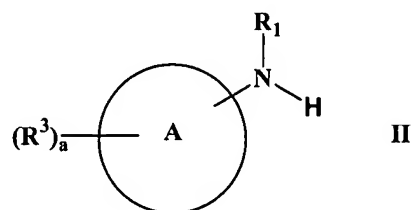
(1) halogenating a carboxylic acid of formula VI with a halogenating agent:



to form an acid halide of formula VII:

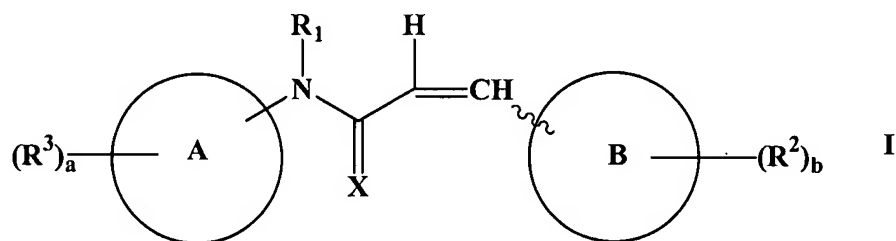


(2) coupling the acid halide VII to an aromatic amino compound of formula II



to form an amide compound of formula I;
or a salt of such a compound.

26. (withdrawn) A process for preparing a compound according to claim 2, which compound has the formula I,

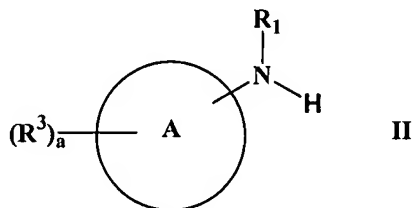


wherein:

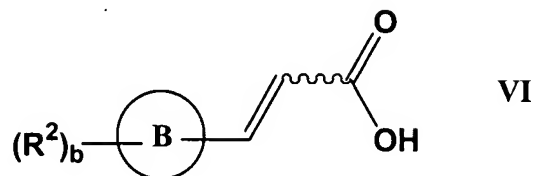
R^1 , R^2 , R^3 , a, b, X, A and B are as defined in claim 2;

comprising:

reacting an aromatic amino compound of formula II

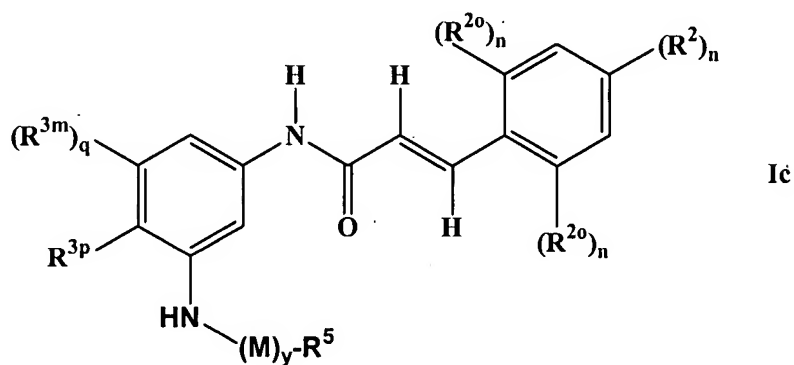


with a carboxylic acid compound of formula VI:



and an amide coupling agent, to form a compound of formula I;
or a salt of such a compound.

27. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



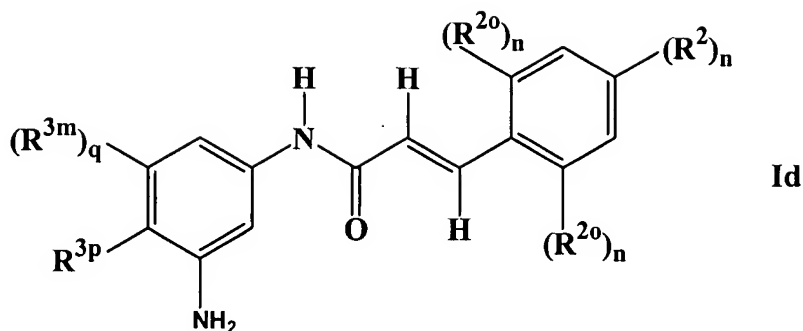
wherein:

q is 0 or 1; and

R^2 , R^{2o} , R^{3m} , R^{3p} , n, M, y and R^6 are defined as in claim 21;

comprising:

reacting an aromatic amino compound of formula Id



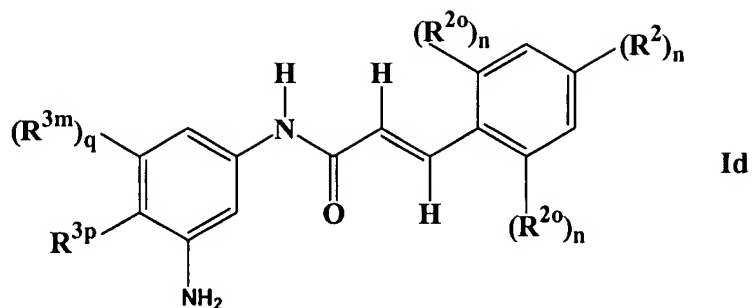
with an electrophilic compound of formula VIII:



wherein R⁵ comprises an electrophilic reactive center selected from the group consisting of:

- (a) an alkyl moiety having a leaving group;
 - (b) an aryl or heteroaryl halide or aryl or heteroaryl pseudo halide;
 - (c) a carboxylic acid activated with a leaving group;
 - (d) a sulfonic acid activated with a leaving group;
 - (e) a carbamic acid moiety activated with a leaving group;
 - (f) a cyanate moiety;
 - (g) an aldehyde or ketone moiety, or a hydrate thereof or a ketal or acetal thereof;
 - (h) a carboxylic acid moiety and an amide coupling reagent; or
 - (i) the intermediate product of a thiourea moiety and 2-chloro-1-methyl pyridinium iodide;
- to form a compound of formula Ic,
or a salt of such a compound.

28. (withdrawn) A process for preparing a compound according to claim 23, which compound has the formula Id:



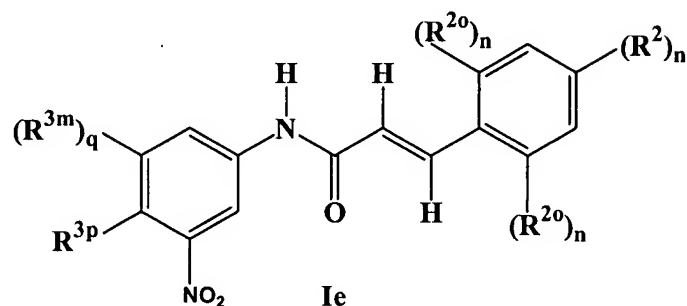
wherein:

q is 0 or 1; and

R^2 , R^{2o} , R^{3m} , R^{3p} and n are defined as in claim 23;

comprising:

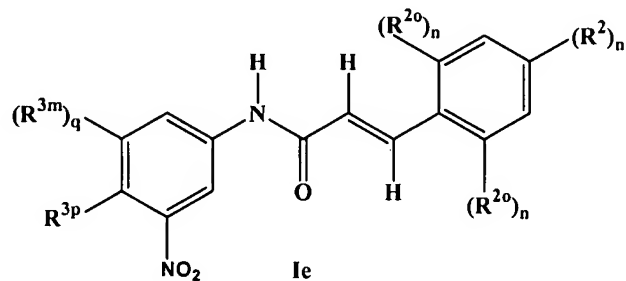
chemically reducing a compound of formula Ie:



to form a compound of formula Id,

or a salt of such a compound.

29. (withdrawn) A process for preparing a compound according to claim 16, which compound has the formula Ie:



wherein:

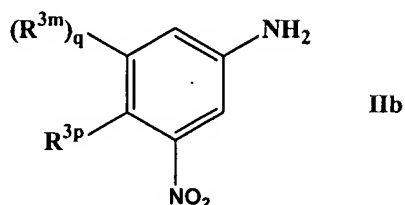
q is 0 or 1; and

R^2 , R^{2o} , R^{3m} , R^{3p} and n are defined as in claim 16; and

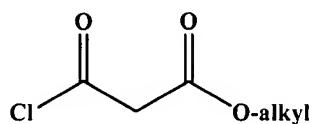
the olefin double bond is in the *E* conformation;

comprising:

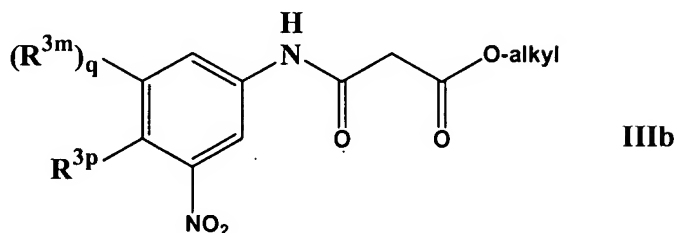
(1) coupling a compound of formula IIb:



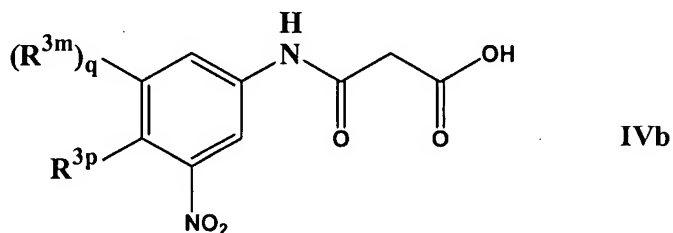
with an alkyl ester of malonic acid chloride:



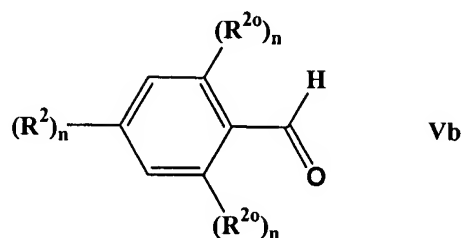
to yield a carboxylic ester compound of formula IIIb:



(2) hydrolyzing the carboxylic ester compound of formula IIIb to form a carboxylic acid compound of formula IVb; and

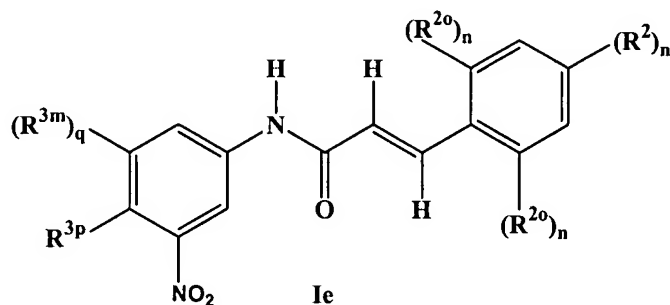


(3) coupling of the carboxylic acid compound of formula IVb with an aromatic aldehyde of formula V:



in glacial acetic acid at elevated temperature to form a compound of formula Ie;
or a salt of such a compound.

30. (withdrawn) A process for preparing a compound according to claim 16, which compound has the formula Ie:



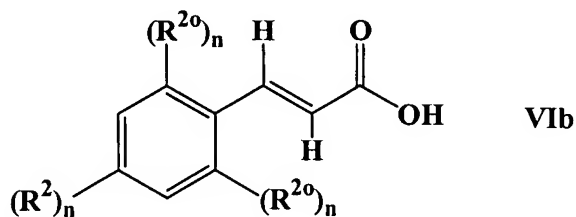
wherein:

q is 0 or 1; and

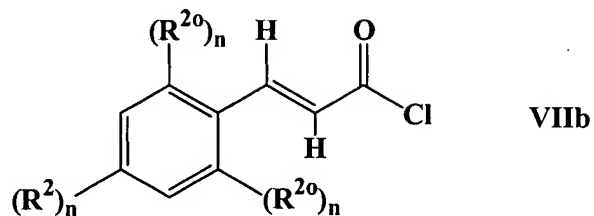
R^2 , R^{2o} , R^{3m} , R^{3p} and n are defined as in claim 16;

comprising:

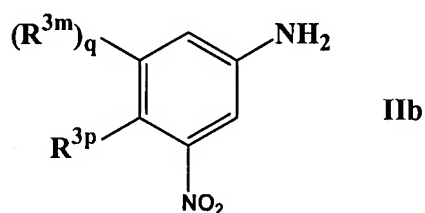
(1) halogenating a carboxylic acid of formula VIb with a halogenating agent:



to form an acid halide of formula VIIb:

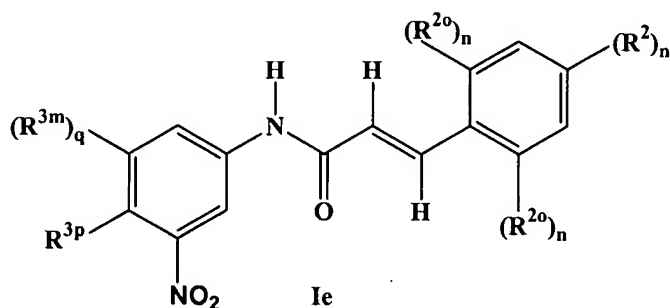


(2) coupling the acid halide VIIb to an aromatic amino compound of formula IIb



to form an amide compound of formula Ie;
or a salt of such a compound.

31. (withdrawn) A process for preparing a compound according to claim 16, which compound has the formula Ie:



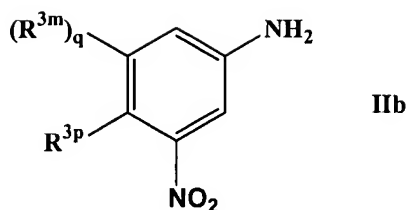
wherein:

q is 0 or 1; and

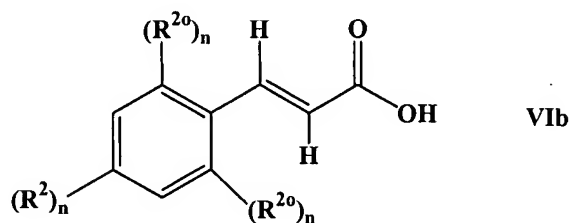
R^2 , R^{2o} , R^{3m} , R^{3p} and n are defined as in claim 16;

comprising:

(1) reacting an aromatic amino compound of formula IIb

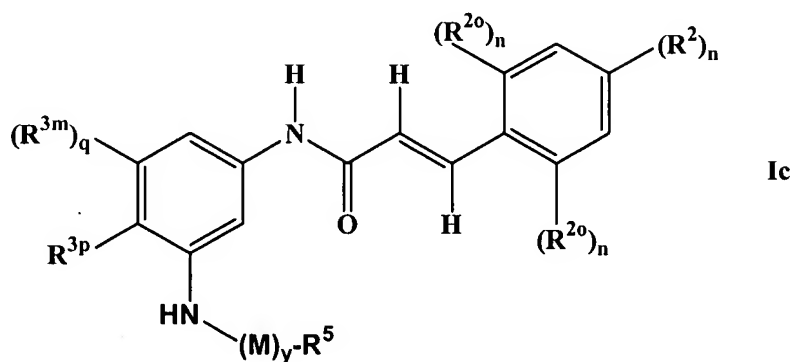


with a carboxylic acid compound of formula VIb:



and an amide coupling agent,
to form a compound of formula Ic;
or a salt of such a compound.

32. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



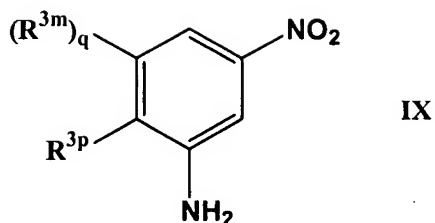
wherein:

q is 0 or 1; and

R^2 , R^{2o} , R^{3m} , R^{3p} , n, M, y and R^5 are defined as in claim 21;

comprising:

(1) reacting an aromatic amine of formula IX



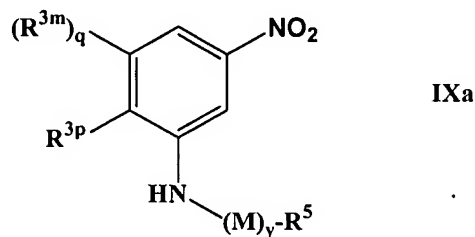
with an electrophilic compound of formula VIII:



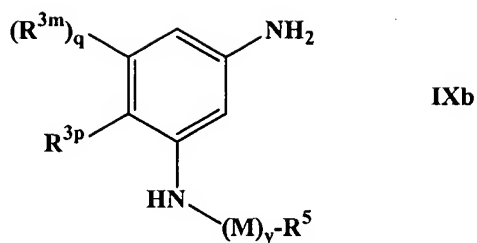
wherein L comprises an electrophilic reactive center selected from the group consisting of:

- (a) an alkyl moiety having a leaving group;
- (b) an aryl or heteroaryl halide or aryl or heteroaryl pseudo halide;
- (c) a carboxylic acid activated with a leaving group;
- (d) a sulfonic acid activated with a leaving group;
- (e) a carbamic acid moiety activated with a leaving group;
- (f) a cyanate moiety;
- (g) an aldehyde or ketone moiety, or a hydrate thereof or a ketal or acetal thereof;
- (h) a carboxylic acid moiety and an amide coupling reagent; or
- (i) the intermediate product of a thiourea moiety and 2-chloro-1-methyl pyridinium iodide;

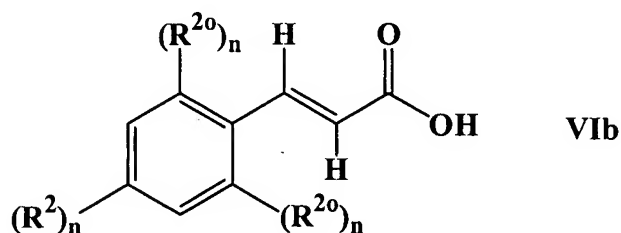
to form a compound of formula IXa:



- (2) optionally protecting the $\text{--NH--(M)}_y\text{--R}^5$ moiety in the formula IXa compound;
- (3) chemically reducing said compound of formula IXa to form the aromatic amine IXb:



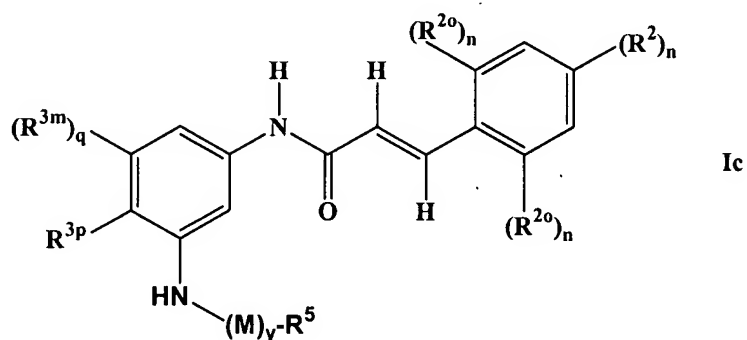
(4) reacting aromatic amine IXb with a carboxylic acid compound of formula VIb:



and an amide coupling agent; and

(5) optionally removing said protecting group to form a compound of formula Ic;
or a salt of such a compound.

33. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



wherein:

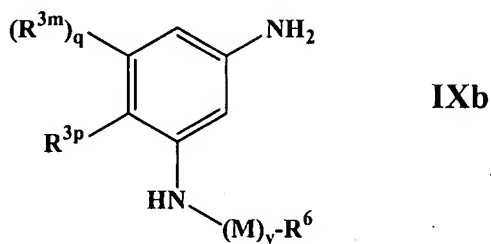
q is 0 or 1;

R^2 , R^{2o} , R^{3m} , R^{3p} , n, M, y and R^5 are defined as in claim 21; and

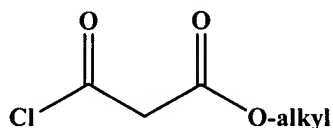
the olefin double bond is in the *E* conformation;

comprising:

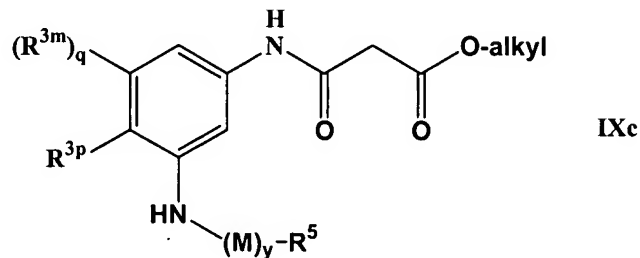
(1) coupling a compound of formula IXb:



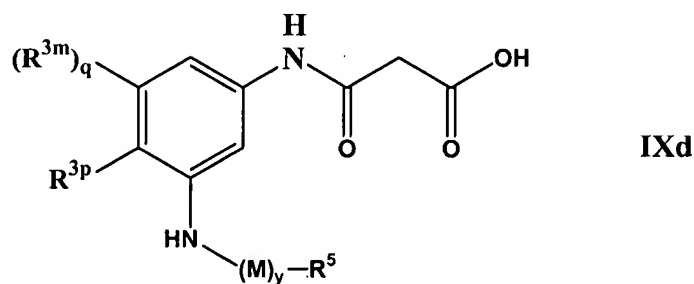
wherein the $\text{-NH-(M)}_y\text{-R}^5$ moiety is optionally protected with a protecting group;
with an alkyl ester of malonic acid chloride:



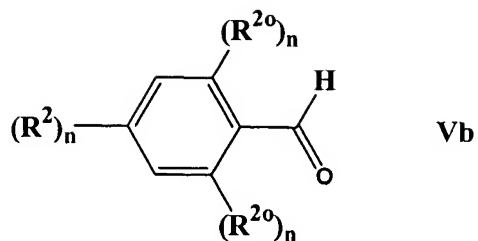
to yield a carboxylic ester compound of formula IXc:



(2) hydrolyzing the carboxylic ester compound of formula IXc to form a carboxylic acid compound of formula IXd;



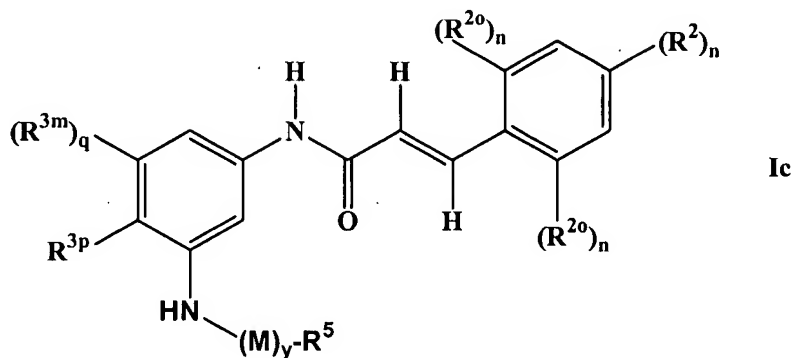
(3) coupling the carboxylic acid compound of formula IXd with an aromatic aldehyde of formula Vb:



in glacial acetic acid at elevated temperature; and

(4) optionally removing said protecting group to form a compound of formula Ic;
or a salt of such a compound.

34. (withdrawn) A process for preparing a compound according to claim 21, which compound has the formula Ic:



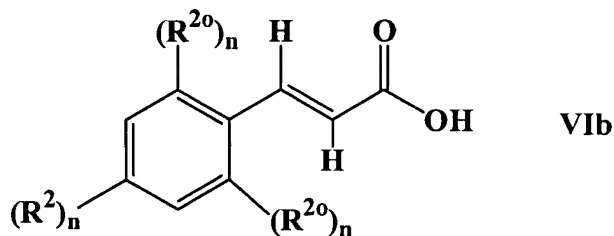
wherein:

q is 0 or 1; and

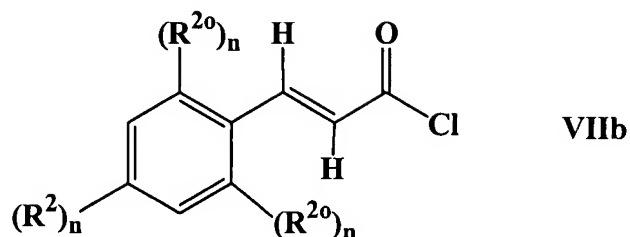
R^2 , R^{2o} , R^{3m} , R^{3p} , n, M, y and R^5 are defined as in claim 21;

comprising:

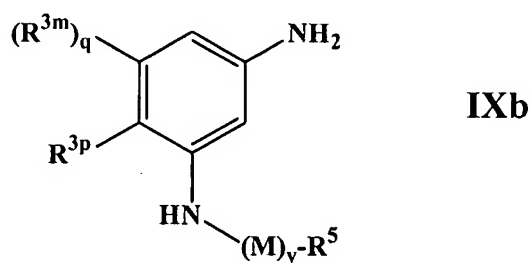
(1) halogenating a carboxylic acid of formula VIb with a halogenating agent:



to form an acid halide of formula VIIb:



(2) coupling the acid halide VIIb to an aromatic amino compound of formula IXb:



wherein the $\text{--NH--(M)}_y\text{--R}^5$ moiety is optionally protected with a protecting group;

and

(3) optionally removing said protecting group to form an amide compound of formula Ic;
or a salt of such a compound.

35. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one compound according to claim 1.

36. (cancelled)

37. (withdrawn) A conjugate of the formula, I-L-Ab;
wherein:

I is a compound according to claim 1;

Ab is an antibody; and

—L— is a single covalent bond or a linking group covalently linking said compound to said antibody.

38-41. (cancelled)

42. (withdrawn) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and at least one conjugate according to claim 37.

43. (previously presented) A method of treating an individual for a proliferative disorder comprising administering to said individual an effective amount of at least one compound according to claim 1, or a salt thereof.

44. (cancelled)

45. (previously presented) A method according to claim 43 wherein the proliferative disorder is selected from the group consisting of hemangiomas in newborn; secondary progressive multiple sclerosis; chronic progressive myelodegenerative disease; neurofibromatosis; ganglioneuromatosis; keloid formation; Paget's disease of the bone; fibrocystic disease; sarcoidosis; Peyronie's fibrosis; Dupuytren's fibrosis; cirrhosis, atherosclerosis and vascular restenosis.

46. (original) A method according to claim 45 wherein the proliferative disorder is cancer.

47. (original) A method of according to claim 46 wherein the cancer is selected from the group of ovarian cancer, breast cancer, prostate cancer, lung cancer, renal cancer, colorectal cancer, brain cancer and leukemia.

48-49. (cancelled)

50. (previously presented) A method of selectively inducing apoptosis of tumor cells in an individual afflicted with cancer comprising administering to said individual an effective amount of at least one compound according to claim 1, or a salt thereof.

51. (cancelled)

52. (original) A method according to claim 50 wherein the tumor cells are selected from the group of tumors consisting of tumors of the ovarian, breast, prostate, lung, colorectal, renal and brain tumors

53. (withdrawn) A method of treating an individual afflicted with cancer, comprising administering to said individual an effective amount of at least one conjugate according to claim 37.

54. (previously presented): A method of reducing or eliminating the effects of ionizing radiation on normal cells in a subject who has incurred or is at risk of incurring exposure to ionizing radiation, comprising administering to the subject an effective amount of at least one radioprotective compound according to claim 1, or a salt thereof, to the subject prior to or after exposure to ionizing radiation.

55. (cancelled)

56. (original) The method of claim 54 wherein the radioprotective compound is administered before the subject is exposed to the ionizing radiation.

57-59. (cancelled)

60. (original) The method of claim 54 wherein the radioprotective compound is administered after the subject is exposed to the ionizing radiation.

61. (cancelled)

62. (previously presented) A method of reducing the number of malignant cells in bone marrow of a subject, comprising:

- (1) removing a portion of the subject's bone marrow;
- (2) administering an effective amount of at least one radioprotective aryl or heteroaryl propene amide according to claim 1 or a salt of such a compound to the removed bone marrow; and
- (3) irradiating the removed bone marrow with an effective amount of ionizing radiation.

63-67. (cancelled)

68. (previously presented) A method for protecting an animal from cytotoxic side effects of the administration of a mitotic phase cell cycle inhibitor or a topoisomerase inhibitor comprising administering to the animal, in advance of administration of said inhibitor, an effective amount of at least one cytoprotective aryl or heteroaryl propene amide according to claim 1, or a salt thereof, wherein the mitotic phase cell cycle inhibitor or topoisomerase inhibitor is other than a compound according to claim 1, or a salt thereof.

69. (cancelled)

70. (original) The method according to claim 68 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of vinca alkaloids, taxanes, naturally occurring macrolides, and colchicine and its derivatives.

71-75. (cancelled)

76. (previously presented) A method for treating cancer or other proliferative disorder comprising administering to an animal an effective amount at least one cytoprotective compound according to claim 1-or a salt of such a compound; followed by an effective amount of at least one mitotic phase cell cycle inhibitor or topoisomerase inhibitor after administration of the cytoprotective compound.

77. (original) The method according to claim 76 wherein the mitotic phase cell cycle inhibitor is selected from the group consisting of vinca alkaloids, taxanes, naturally occurring macrolides, and colchicine and its derivatives.

78-82. (cancelled)

83. (withdrawn) A compound according to claim 21, wherein:

M is $-(C_1-C_6)\text{alkylene}-$;

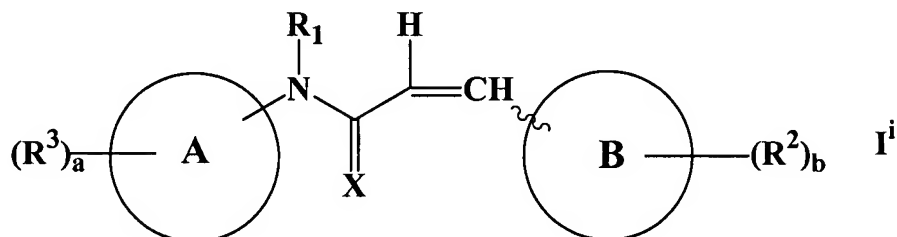
y is 1;

R^4 is $-H$ or $-(C_1-C_6)\text{alkyl}$;

R^5 is $-\text{CO}_2R^4$; and

Q is 0; or a salt of such a compound.

84. (currently amended) A method of treating an individual for a proliferative disorder comprising administering to said individual an effective amount of at least one compound according to formula Iⁱ,



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

R¹ is independently selected from the group consisting of -R⁴, -SO₂(C₁-C₆)alkyl, -C(=O)R⁴, -C(=O)OR⁴, -C(=O)O(C₁-C₆)alkylenearyl, -OR⁴, -(C₂-C₆)alkynyl, -(C₃-C₆)heteroalkenyl, -(C₂-C₆)alkylene-OR⁴, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C₁-C₃)alkyl, unsubstituted aryl(C₁-C₃)alkyl, substituted heteroaryl(C₁-C₃)alkyl and unsubstituted heteroaryl(C₁-C₃)alkyl;

R² is independently selected from -(C₁-C₆)alkyl, halogen, -OR⁴, -C≡N, -NO₂, -CO₂R⁴, -C(=O)NR⁴₂, -C(=NR⁴)NR⁴₂, -O(C₁-C₃)alkylene-CO₂R⁴, -(C₂-C₆)alkylene-OR⁴, phosphonato, -NR⁴₂, -NHC(=O)(C₁-C₆)alkyl, sulfamyl, carbamyl, -OC(=O)(C₁-C₃)alkyl, -O(C₂-C₆)alkylene-N((C₁-C₆)alkyl)₂, -S(C₁-C₃)alkyl, -S(=O)(C₁-C₃)alkyl—and, (C₁-C₃)perfluoroalkyl and -SO₂(C₁-C₃)alkyl;

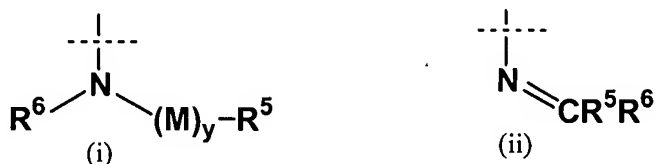
b is 1, 2, 3, 4 or 5; and

~~~~~; indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R<sup>3</sup> is independently selected from halogen, -(C<sub>1</sub>-C<sub>6</sub>)alkyl, -OR<sup>4</sup>, -C≡N, -C(=NR<sup>4</sup>)NR<sup>4</sup><sub>2</sub>, -O(C<sub>1</sub>-C<sub>3</sub>)alkylene-CO<sub>2</sub>R<sup>4</sup>, -(C<sub>1</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, nitro, phosphonato, -NHC(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl,



sulfamyl,  $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_3)\text{alkyl}$ ,  $-\text{O}(\text{C}_2\text{-C}_6)\text{alkylene-N}((\text{C}_1\text{-C}_6)\text{alkyl})_2$ ,  $-(\text{C}_1\text{-C}_3)\text{perfluoroalkyl}$  and (i) and or (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of  $-(\text{C}_1\text{-C}_6)\text{alkylene-}$ ,  $-(\text{CH}_2)_d\text{-V}-(\text{CH}_2)_e\text{-}$ ,  $-(\text{CH}_2)_f\text{-W}-(\text{CH}_2)_g\text{-}$  and  $-\text{Z-}$ ;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene,  $-\text{C}(=\text{O})\text{-}$ ,  $-\text{C}(=\text{O})(\text{C}_1\text{-C}_6)\text{perfluoroalkylene-}$ ,  $-\text{C}(=\text{O})\text{-}$ ,  $-\text{C}(=\text{S})\text{-}$ ,  $-\text{S}(=\text{O})\text{-}$ ,  $-\text{SO}_2\text{-}$ ,  $-\text{C}(=\text{O})\text{NR}^4\text{-}$ ,  $-\text{C}(=\text{S})\text{NR}^4\text{-}$  and  $-\text{SO}_2\text{NR}^4\text{-}$ ;

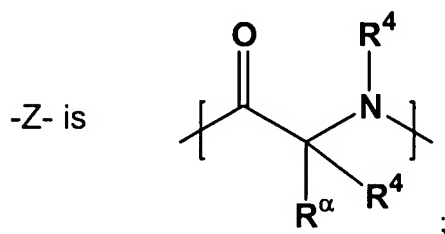
each W is independently selected from the group consisting of  $-\text{NR}^4\text{-}$ ,  $-\text{O-}$  and  $-\text{S-}$ ;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of  $-\text{Z-}$  is S or R, or a mixture of S and R;

each  $\text{R}^a$  is independently selected from the group consisting of  $-\text{H}$ ,  $-(\text{C}_1\text{-C}_6)\text{alkyl}$ ,  $-(\text{CH}_2)_3\text{-NH-C}(\text{NH}_2)(=\text{NH})$ ,  $-\text{CH}_2\text{C}(=\text{O})\text{NH}_2$ ,  $-\text{CH}_2\text{COOH}$ ,  $-\text{CH}_2\text{SH}$ ,  $-(\text{CH}_2)_2\text{C}(=\text{O})\text{-NH}_2$ ,  $-(\text{CH}_2)_2\text{COOH}$ ,  $-\text{CH}_2\text{-(2-imidazolyl)}$ ,  $-(\text{CH}_2)_4\text{-NH}_2$ ,  $-(\text{CH}_2)_2\text{-S-CH}_3$ , phenyl,  $-\text{CH}_2\text{-phenyl}$ ,  $-\text{CH}_2\text{-}$

OH, -CH(OH)-CH<sub>3</sub>, -CH<sub>2</sub>-(3-indolyl), -CH<sub>2</sub>-(4-hydroxyphenyl); and includes compounds wherein R<sup>a</sup> and R<sup>4</sup> combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R<sup>4</sup> is independently selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>6</sub>)alkyl, substituted -(C<sub>1</sub>-C<sub>6</sub>)alkyl, -(C<sub>2</sub>-C<sub>6</sub>)alkenyl, substituted -(C<sub>2</sub>-C<sub>6</sub>)alkenyl and heteroalkyl, wherein two R<sup>4</sup> groups may together form a heterocycle;

each R<sup>5</sup> is independently selected from the group consisting of -R<sup>4</sup>, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)NR<sup>4</sup><sub>2</sub>, -C(=NH)-NR<sup>4</sup><sub>2</sub>, -(C<sub>1</sub>-C<sub>6</sub>)perfluoroalkyl, -CF<sub>2</sub>Cl, -P(=O)(OR<sup>4</sup>)<sub>2</sub>, -OP(=O)(OR<sup>4</sup>)<sub>2</sub>, -CR<sup>4</sup>R<sup>7</sup>R<sup>8</sup> and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R<sup>5</sup> is -CO<sub>2</sub>R<sup>4</sup>; then R<sup>4</sup> is not -H;

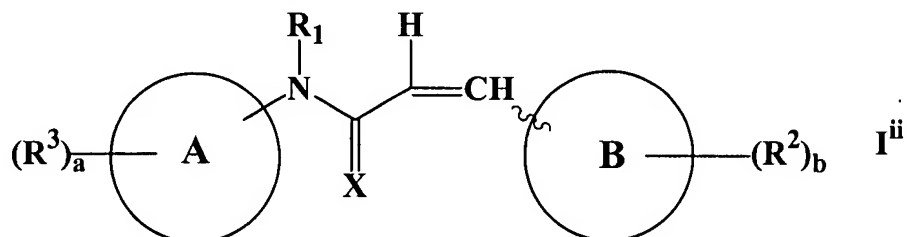
each R<sup>6</sup> is independently selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>6</sub>)alkyl, and aryl(C<sub>1</sub>-C<sub>3</sub>)alkyl;

each R<sup>7</sup> is independently selected from the group consisting of -H, -(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(=O)R<sup>8</sup>, -OR<sup>4</sup>, -SR<sup>4</sup>, -OC(=O)(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>R<sup>6</sup>, guanidino, -NR<sup>4</sup><sub>2</sub>, -NR<sup>4</sup><sub>3</sub><sup>+</sup>, -N<sup>+</sup>(CH<sub>2</sub>CH<sub>2</sub>OR<sup>5</sup>)<sub>3</sub>, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R<sup>8</sup> is independently selected from the group consisting of R<sup>a</sup>, halogen, -NR<sup>4</sup><sub>2</sub> and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within [[Ar,]] R<sup>1</sup>, R<sup>5</sup> [[R<sup>6</sup>,]] and R<sup>7</sup> ~~and~~ R<sup>a</sup> are independently selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, -NO<sub>2</sub>, -C≡N, -C(=O)O(C<sub>1</sub>-C<sub>3</sub>)alkyl, -OR<sup>4</sup>, -(C<sub>2</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, phosphonato, -NR<sup>4</sup><sub>2</sub>, -NHC(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl, sulfamyl, carbamyl, -OC(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, -O(C<sub>2</sub>-C<sub>6</sub>)alkylene-N((C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub> and -(C<sub>1</sub>-C<sub>3</sub>)perfluoroalkyl; or a salt of such a compound.

85. (currently amended) A method of selectively inducing apoptosis of tumor cells in an individual afflicted with cancer comprising administering to said individual an effective amount of at least one compound according to formula I<sup>ii</sup>



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

R<sup>1</sup> is independently selected from the group consisting of -R<sup>4</sup>, -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(=O)R<sup>4</sup>, -C(=O)OR<sup>4</sup>, -C(=O)O(C<sub>1</sub>-C<sub>6</sub>)alkylenearyl, -OR<sup>4</sup>, -(C<sub>2</sub>-C<sub>6</sub>)alkynyl, -(C<sub>3</sub>-C<sub>6</sub>)heteroalkenyl, -(C<sub>2</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C<sub>1</sub>-C<sub>3</sub>)alkyl, unsubstituted aryl(C<sub>1</sub>-C<sub>3</sub>)alkyl, substituted heteroaryl(C<sub>1</sub>-C<sub>3</sub>)alkyl and unsubstituted heteroaryl(C<sub>1</sub>-C<sub>3</sub>)alkyl;

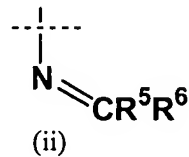
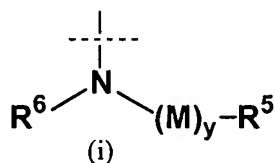
R<sup>2</sup> is independently selected from -(C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, -OR<sup>4</sup>, -C≡N, -NO<sub>2</sub>, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)NR<sup>4</sup><sub>2</sub>, -C(=NR<sup>4</sup>)NR<sup>4</sup><sub>2</sub>, -O(C<sub>1</sub>-C<sub>3</sub>)alkylene-CO<sub>2</sub>R<sup>4</sup>, -(C<sub>2</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, phosphonato, -NR<sup>4</sup><sub>2</sub>, -NHC(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl, sulfamyl, carbamyl, -OC(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, -O(C<sub>2</sub>-C<sub>6</sub>)alkylene-N((C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub>, -S(C<sub>1</sub>-C<sub>3</sub>)alkyl, -S(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, -(C<sub>1</sub>-C<sub>3</sub>)perfluoroalkyl and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>)alkyl;

b is 1, 2, 3, 4 or 5; and

~~~~ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R³ is independently selected from halogen, -(C₁-C₆)alkyl, -OR⁴, -C≡N, -C(=O)NR⁴₂, -C(=O)OR⁴, -C(=NR⁴)NR⁴₂, -O(C₁-C₃)alkylene-CO₂R⁴, -(C₁-C₆)alkylene-OR⁴, nitro,

phosphonato, $-\text{NHC}(=\text{O})(\text{C}_1\text{-C}_6)\text{alkyl}$, sulfamyl, $-\text{OC}(=\text{O})(\text{C}_1\text{-C}_3)\text{alkyl}$, $-\text{O}(\text{C}_2\text{-C}_6)\text{alkylene-}$
 $\text{N}((\text{C}_1\text{-C}_6)\text{alkyl})_2$, $-(\text{C}_1\text{-C}_3)\text{perfluoroalkyl}$ and (i) and or (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of $-(\text{C}_1\text{-C}_6)\text{alkylene-}$, $-(\text{CH}_2)_d\text{-V-}(\text{CH}_2)_e\text{-}$, $-(\text{CH}_2)_f\text{-W-}(\text{CH}_2)_g\text{-}$ and $-\text{Z-}$;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, $-\text{C}(=\text{O})\text{-}$, $-\text{C}(=\text{O})(\text{C}_1\text{-C}_6)\text{perfluoroalkylene-}$, $-\text{C}(=\text{O})\text{-}$, $-\text{C}(=\text{S})\text{-}$, $-\text{S}(=\text{O})\text{-}$, $-\text{SO}_2\text{-}$, $-\text{C}(=\text{O})\text{NR}^4\text{-}$, $-\text{C}(=\text{S})\text{NR}^4\text{-}$ and $-\text{SO}_2\text{NR}^4\text{-}$;

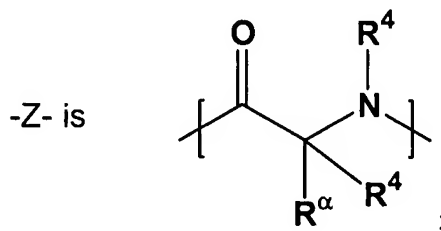
each W is independently selected from the group consisting of $-\text{NR}^4\text{-}$, $-\text{O-}$ and $-\text{S-}$;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of $-\text{Z-}$ is S or R, or a mixture of S and R;

each R^α is independently selected from the group consisting of $-\text{H}$, $-(\text{C}_1\text{-C}_6)\text{alkyl}$, $-(\text{CH}_2)_3\text{-NH-C}(\text{NH}_2)(=\text{NH})$, $-\text{CH}_2\text{C}(=\text{O})\text{NH}_2$, $-\text{CH}_2\text{COOH}$, $-\text{CH}_2\text{SH}$, $-(\text{CH}_2)_2\text{C}(=\text{O})\text{-NH}_2$, $-(\text{CH}_2)_2\text{COOH}$, $-\text{CH}_2\text{-(2-imidazolyl)}$, $-(\text{CH}_2)_4\text{-NH}_2$, $-(\text{CH}_2)_2\text{-S-CH}_3$, phenyl, $-\text{CH}_2\text{-phenyl}$, $-\text{CH}_2\text{-}$

OH, -CH(OH)-CH₃, -CH₂-(3-indolyl), -CH₂-(4-hydroxyphenyl); and includes compounds wherein R^a and R⁴ combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R⁴ is independently selected from the group consisting of -H, -(C₁-C₆)alkyl, substituted -(C₁-C₆)alkyl, -(C₂-C₆)alkenyl, substituted -(C₂-C₆)alkenyl and heteroalkyl, wherein two R⁴ groups may together form a heterocycle;

each R⁵ is independently selected from the group consisting of -R⁴, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, -CO₂R⁴, -C(=O)NR⁴₂, -C(=NH)-NR⁴₂, -(C₁-C₆)perfluoroalkyl, -CF₂Cl, -P(=O)(OR⁴)₂, -OP(=O)(OR⁴)₂, -CR⁴R⁷R⁸ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R⁵ is -CO₂R⁴; then R⁴ is not -H;

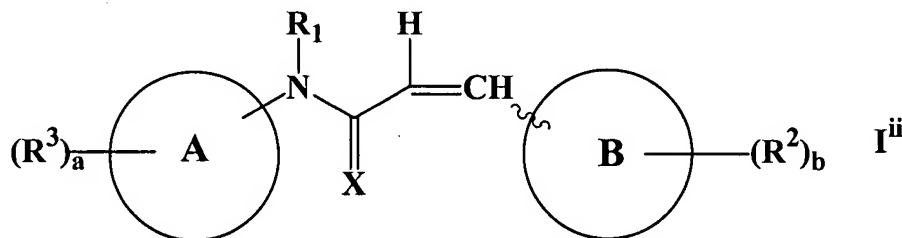
each R⁶ is independently selected from the group consisting of -H, -(C₁-C₆)alkyl, and aryl(C₁-C₃)alkyl;

each R⁷ is independently selected from the group consisting of -H, -(C₁-C₆)alkyl, -C(=O)R⁸, -OR⁴, -SR⁴, -OC(=O)(CH₂)₂CO₂R⁶, guanidino, -NR⁴₂, -NR⁴₃⁺, -N⁺(CH₂CH₂OR⁵)₃, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R⁸ is independently selected from the group consisting of R^a, halogen, -NR⁴₂ and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within [[Ar,]] R¹, R⁵ [[R⁶,]] and R⁷ and R^a are independently selected from the group consisting of halogen, -(C₁-C₆)alkyl, -(C₁-C₆)alkoxy, -NO₂, -C≡N, -C(=O)O(C₁-C₃)alkyl, -OR⁴, -(C₂-C₆)alkylene-OR⁴, phosphonato, -NR⁴₂, -NHC(=O)(C₁-C₆)alkyl, sulfamyl, carbamyl, -OC(=O)(C₁-C₃)alkyl, -O(C₂-C₆)alkylene-N((C₁-C₆)alkyl)₂ and -(C₁-C₃)perfluoroalkyl; or a salt of such a compound.

86. (currently amended): A method of reducing or eliminating the effects of ionizing radiation on normal cells in a subject who has incurred or is at risk of incurring exposure to ionizing radiation, comprising administering to the subject an effective amount of at least one radioprotective compound according to formula Iⁱⁱ to the subject prior to or after exposure to ionizing radiation:



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

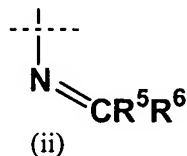
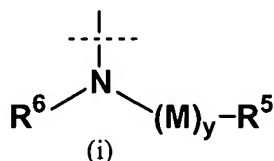
R¹ is independently selected from the group consisting of -R⁴, -SO₂(C₁-C₆)alkyl, C(=O)R⁴, -C(=O)OR⁴, -C(=O)O(C₁-C₆)alkylenearyl, -OR⁴, -(C₂-C₆)alkynyl, -(C₃-C₆)heteroalkenyl, -(C₂-C₆)alkylene-OR⁴, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C₁-C₃)alkyl, unsubstituted aryl(C₁-C₃)alkyl, substituted heteroaryl(C₁-C₃)alkyl and unsubstituted heteroaryl(C₁-C₃)alkyl;

R² is independently selected from -(C₁-C₆)alkyl, halogen, -OR⁴, -C≡N, -NO₂, -CO₂R⁴, -C(=O)NR⁴₂, -C(=NR⁴)NR⁴₂, -O(C₁-C₃)alkylene-CO₂R⁴, -(C₂-C₆)alkylene-OR⁴, phosphonato, -NR⁴₂, -NHC(=O)(C₁-C₆)alkyl, sulfamyl, carbamyl, -OC(=O)(C₁-C₃)alkyl, -O(C₂-C₆)alkylene-N((C₁-C₆)alkyl)₂, -S(C₁-C₃)alkyl, -S(=O)(C₁-C₃)alkyl (C₁-C₃)perfluoroalkyl and -SO₂(C₁-C₃)alkyl;

b is 1, 2, 3, 4 or 5; and

~~~~~ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

$R^3$  is independently selected from halogen,  $-(C_1-C_6)alkyl$ ,  $-OR^4$ ,  $-C\equiv N$ ,  $-C(=O)NR^4_2$ ,  $-C(=O)OR^4$ ,  $-C(=NR^4)NR^4_2$ ,  $-O(C_1-C_3)alkylene-CO_2R^4$ ,  $-(C_1-C_6)alkylene-OR^4$ , nitro, phosphonato,  $-NHC(=O)(C_1-C_6)alkyl$ , sulfamyl, carbamyl,  $-OC(=O)(C_1-C_3)alkyl$ ,  $-O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)_2$ ,  $-(C_1-C_3)perfluoroalkyl$  and (i) and (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of  $-(C_1-C_6)alkylene-$ ,  $-(CH_2)_d-V-(CH_2)_e-$ ,  $-(CH_2)_f-W-(CH_2)_g-$  and  $-Z-$ ;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene,  $-C(=O)-$ ,  $-C(=O)(C_1-C_6)perfluoroalkylene-$ ,  $-C(=O)-$ ,  $-C(=S)-$ ,  $-S(=O)-$ ,  $-SO_2-$ ,  $-C(=O)NR^4-$ ,  $-C(=S)NR^4-$  and  $-SO_2NR^4-$ ;

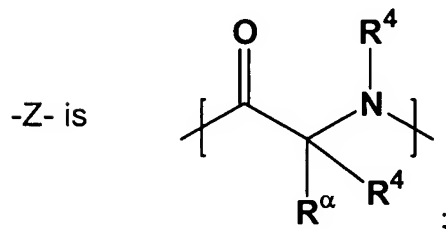
each W is independently selected from the group consisting of  $-NR^4-$ ,  $-O-$  and  $-S-$ ;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of  $-Z-$  is S or R, or a mixture of S and R;

each  $R^a$  is independently selected from the group consisting of  $-H$ ,  $-(C_1-C_6)alkyl$ ,  $-(CH_2)_3-NH-C(NH_2)(=NH)$ ,  $-CH_2C(=O)NH_2$ ,  $-CH_2COOH$ ,  $-CH_2SH$ ,  $-(CH_2)_2C(=O)-NH_2$ ,  $-(CH_2)_2COOH$ ,  $-CH_2-(2-imidazolyl)$ ,  $-(CH_2)_4-NH_2$ ,  $-(CH_2)_2-S-CH_3$ , phenyl,  $CH_2$ -phenyl,  $-CH_2-OH$ ,  $-CH(OH)-CH_3$ ,  $-CH_2-(3-indolyl)$ ,  $-CH_2-(4-hydroxyphenyl)$ ; and includes compounds wherein  $R^a$  and  $R^4$  combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

$R^4$  is independently selected from the group consisting of  $-H$ ,  $-(C_1-C_6)alkyl$ , substituted  $-(C_1-C_6)alkyl$ ,  $-(C_2-C_6)alkenyl$ , substituted  $-(C_2-C_6)alkenyl$  and heteroalkyl, wherein two  $R^4$  groups may together form a heterocycle;

each  $R^5$  is independently selected from the group consisting of  $-R^4$ , unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic,  $-CO_2R^4$ ,  $-C(=O)NR^4_2$ ,  $-C(=NH)-NR^4_2$ ,  $-(C_1-C_6)perfluoroalkyl$ ,  $-CF_2Cl$ ,  $-P(=O)(OR^4)_2$ ,  $-OP(=O)(OR^4)_2$ ,  $-CR^4R^7R^8$  and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and  $R^5$  is  $-CO_2R^4$ ; then  $R^4$  is not  $-H$ ;

each  $R^6$  is independently selected from the group consisting of  $-H$ ,  $-(C_1-C_6)alkyl$ , and  $aryl(C_1-C_3)alkyl$ ;

each  $R^7$  is independently selected from the group consisting of  $-H$ ,  $-(C_1-C_6)alkyl$ ,  $-C(=O)R^8$ ,  $-OR^4$ ,  $-SR^4$ ,  $-OC(=O)(CH_2)_2CO_2R^6$ , guanidino,  $-NR^4_2$ ,  $-NR^4_3$ ,  $-N^+(CH_2CH_2OR^5)_3$ , halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each  $R^8$  is independently selected from the group consisting of  $R^a$ , halogen,  $-NR^4_2$  and heterocycles containing two nitrogen atoms;

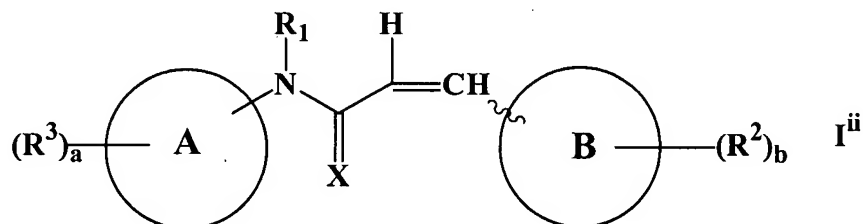
wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within  $[[Ar,]]$   $R^1$ ,  $R^5$   $[[R^6,]]$  and  $R^7$  and  $R^a$  are independently selected from the group consisting of halogen,  $-(C_1-C_6)alkyl$ ,  $-(C_1-C_6)alkoxy$ ,  $-NO_2$ ,  $-C\equiv N$ ,  $-C(=O)O(C_1-C_3)alkyl$ ,  $-OR^4$ ,  $-(C_2-C_6)alkylene-OR^4$ , phosphonato,  $-NR^4_2$ ,  $-NHC(=O)(C_1-C_6)alkyl$ , sulfamyl, carbamyl,  $-OC(=O)(C_1-C_3)alkyl$ ,



-O(C<sub>2</sub>-C<sub>6</sub>)alkylene-N((C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub> and -(C<sub>1</sub>-C<sub>3</sub>)perfluoroalkyl; or a salt of such a compound.

87. (currently amended) A method of reducing the number of malignant cells in bone marrow of a subject, comprising:

- (1) removing a portion of the subject's bone marrow;
- (2) administering an effective amount of at least one radioprotective aryl or heteroaryl propene amide according to formula I<sup>ii</sup>



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

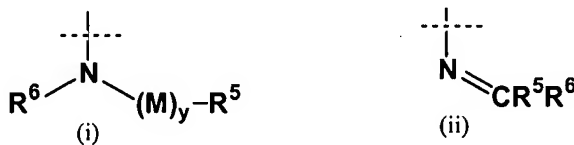
R<sup>1</sup> is independently selected from the group consisting of -R<sup>4</sup>, -SO<sub>2</sub>(C<sub>1</sub>-C<sub>6</sub>)alkyl, -C(=O)R<sup>4</sup>, -C(=O)OR<sup>4</sup>, -C(=O)O(C<sub>1</sub>-C<sub>6</sub>)alkylenearyl, -OR<sup>4</sup>, -(C<sub>2</sub>-C<sub>6</sub>)alkynyl, -(C<sub>3</sub>-C<sub>6</sub>)heteroalkenyl, -(C<sub>2</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl(C<sub>1</sub>-C<sub>3</sub>)alkyl, unsubstituted aryl(C<sub>1</sub>-C<sub>3</sub>)alkyl, substituted heteroaryl(C<sub>1</sub>-C<sub>3</sub>)alkyl and unsubstituted heteroaryl(C<sub>1</sub>-C<sub>3</sub>)alkyl;

R<sup>2</sup> is independently selected from -(C<sub>1</sub>-C<sub>6</sub>)alkyl, halogen, -OR<sup>4</sup>, -C≡N, -NO<sub>2</sub>, -CO<sub>2</sub>R<sup>4</sup>, -C(=O)NR<sup>4</sup><sub>2</sub>, -C(=NR<sup>4</sup>)NR<sup>4</sup><sub>2</sub>, -O(C<sub>1</sub>-C<sub>3</sub>)alkylene-CO<sub>2</sub>R<sup>4</sup>, -(C<sub>2</sub>-C<sub>6</sub>)alkylene-OR<sup>4</sup>, phosphonato, -NR<sup>4</sup><sub>2</sub>, -NHC(=O)(C<sub>1</sub>-C<sub>6</sub>)alkyl, sulfamyl, carbamyl, -OC(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, -O(C<sub>2</sub>-C<sub>6</sub>)alkylene-N((C<sub>1</sub>-C<sub>6</sub>)alkyl)<sub>2</sub>, -S(C<sub>1</sub>-C<sub>3</sub>)alkyl, -S(=O)(C<sub>1</sub>-C<sub>3</sub>)alkyl, -(C<sub>1</sub>-C<sub>3</sub>)perfluoroalkyl and -SO<sub>2</sub>(C<sub>1</sub>-C<sub>3</sub>)alkyl;

b is 1, 2, 3, 4 or 5;

~~~~~ indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R³ is independently selected from halogen, -(C₁-C₆)alkyl, -OR⁴, -C≡N, -C(=O)NR⁴₂, -C(=O)OR⁴, -C(=NR⁴)NR⁴₂, -O(C₁-C₃)alkylene-CO₂R⁴, -(C₁-C₆)alkylene-OR⁴, nitro, phosphonato, -NHC(=O)(C₁-C₆)alkyl, sulfamyl, carbamyl, -OC(=O)(C₁-C₃)alkyl, -O(C₂-C₆)alkylene-N((C₁-C₆)alkyl)₂, -(C₁-C₃)perfluoroalkyl and (i) and (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of -(C₁-C₆)alkylene-, -(CH₂)_d-V-(CH₂)_e-, -(CH₂)_f-W-(CH₂)_g- and -Z-;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, -C(=O)-, -C(=O)(C₁-C₆)perfluoroalkylene, -C(=O)-, -C(=S)-, -S(=O)-, -SO₂-, -C(=O)NR⁴-, -C(=S)NR⁴- and -SO₂NR⁴-;

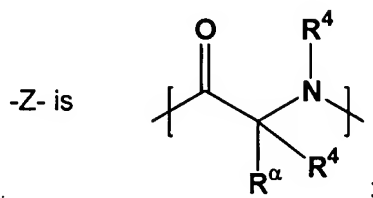
each W is independently selected from the group consisting of -NR⁴-, -O- and -S-;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of -Z- is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, $-(C_1-C_6)\text{alkyl}$, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2-(2\text{-imidazolyl})$, $-(CH_2)_4-NH_2$, $-(CH_2)_2-S-CH_3$, phenyl, $CH_2\text{-phenyl}$, $-CH_2-OH$, $-CH(OH)-CH_3$, $-CH_2-(3\text{-indolyl})$, $-CH_2-(4\text{-hydroxyphenyl})$; and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of -H, $-(C_1-C_6)\text{alkyl}$, substituted $-(C_1-C_6)\text{alkyl}$, $-(C_2-C_6)\text{alkenyl}$, substituted $-(C_2-C_6)\text{alkenyl}$ and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of $-R^4$, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NH)-NR^4_2$, $-(C_1-C_6)\text{perfluoroalkyl}$, $-CF_2Cl$, $-P(=O)(OR^4)_2$, $-OP(=O)(OR^4)_2$, $-CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$, then R^4 is not -H;

each R^6 is independently selected from the group consisting of -H, $-(C_1-C_6)\text{alkyl}$, and $\text{aryl}(C_1-C_3)\text{alkyl}$;

each R^7 is independently selected from the group consisting of -H, $-(C_1-C_6)\text{alkyl}$, $-C(=O)R^8$, $-OR^4$, $-SR^4$, $-OC(=O)(CH_2)_2CO_2R^6$, guanidino, $-NR^4_2$, $-NR^4_3^+$, $-N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

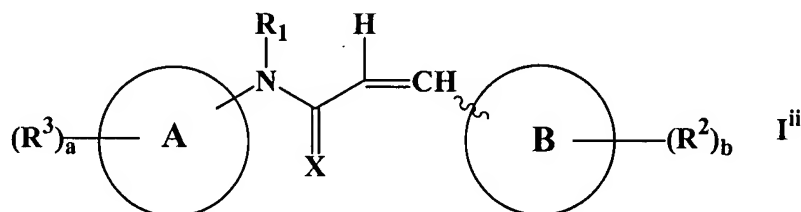
each R^8 is independently selected from the group consisting of R^{α} , halogen, $-NR^4_2$ and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within $[[Ar,]]$ R^1 , R^5 $[[R^6,]]$ and R^7 and $-R^{\alpha}$ are

independently selected from the group consisting of halogen, $-(C_1-C_6)alkyl$, $-(C_1-C_6)alkoxy$, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)alkyl$, $-OR^4$, $-(C_2-C_6)alkylene-OR^4$, phosphonato, $-NR^4_2$, $-NHC(=O)(C_1-C_6)alkyl$, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)alkyl$, $-O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)_2$ and $-(C_1-C_3)perfluoroalkyl$; or a salt of such a compound; and to the removed bone marrow; and

(3) irradiating the removed bone marrow with an effective amount of ionizing radiation.

88. (currently amended) A method for protecting an animal from cytotoxic side effects of the administration of a mitotic phase cell cycle inhibitor or a topoisomerase inhibitor comprising administering to the animal, in advance of administration of said inhibitor, an effective amount of at least one cytoprotective aryl or heteroaryl propene amide according to formula Iⁱⁱ:



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)alkyl$, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)alkylenearyl$, $-OR^4$, $-(C_2-C_6)alkynyl$, $-(C_3-C_6)heteroalkenyl$, $-(C_2-C_6)alkylene-OR^4$, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl $(C_1-C_3)alkyl$, unsubstituted aryl $(C_1-C_3)alkyl$, substituted heteroaryl $(C_1-C_3)alkyl$ and unsubstituted heteroaryl $(C_1-C_3)alkyl$;

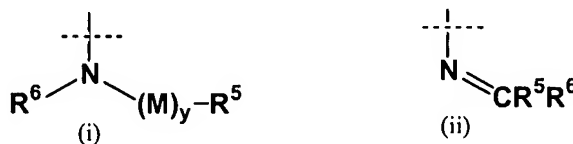
R^2 is independently selected from $-(C_1-C_6)alkyl$, halogen, $-OR^4$, $-C\equiv N$, $-NO_2$, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NR^4)NR^4_2$, $-O(C_1-C_3)alkylene-CO_2R^4$, $-(C_2-C_6)alkylene-OR^4$, phosphonato,

$-\text{NR}^4_2$, $-\text{NHC}(=\text{O})(\text{C}_1-\text{C}_6)\text{alkyl}$, sulfamyl, carbamyl, $-\text{OC}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$, $-\text{O}(\text{C}_2-\text{C}_6)\text{alkylene}-\text{N}((\text{C}_1-\text{C}_6)\text{alkyl})_2$, $-\text{S}(\text{C}_1-\text{C}_3)\text{alkyl}$, $-\text{S}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$, $-(\text{C}_1-\text{C}_3)\text{perfluoroalkyl}$ and $-\text{SO}_2(\text{C}_1-\text{C}_3)\text{alkyl}$;

b is 1, 2, 3, 4 or 5;

\sim indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, $-(\text{C}_1-\text{C}_6)\text{alkyl}$, $-\text{OR}^4$, $-\text{C}\equiv\text{N}$, $-\text{C}(=\text{O})\text{NR}^4_2$, $-\text{C}(=\text{O})\text{OR}^4$, $-\text{C}(=\text{NR}^4)\text{NR}^4_2$, $-\text{O}(\text{C}_1-\text{C}_3)\text{alkylene}-\text{CO}_2\text{R}^4$, $-(\text{C}_1-\text{C}_6)\text{alkylene}-\text{OR}^4$, nitro, phosphonato, $-\text{NHC}(=\text{O})(\text{C}_1-\text{C}_6)\text{alkyl}$, sulfamyl, carbamyl, $-\text{OC}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$, $-\text{O}(\text{C}_2-\text{C}_6)\text{alkylene}-\text{N}((\text{C}_1-\text{C}_6)\text{alkyl})_2$, $-(\text{C}_1-\text{C}_3)\text{perfluoroalkyl}$ and (i) and or (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of $-(\text{C}_1-\text{C}_6)\text{alkylene}-$, $-(\text{CH}_2)_d-\text{V}-(\text{CH}_2)_e-$, $-(\text{CH}_2)_f-\text{W}-(\text{CH}_2)_g-$ and $-\text{Z}-$;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{C}_1-\text{C}_6)\text{perfluoroalkylene}-$, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{S})-$, $-\text{S}(=\text{O})-$, $-\text{SO}_2-$, $-\text{C}(=\text{O})\text{NR}^4-$, $-\text{C}(=\text{S})\text{NR}^4-$ and $-\text{SO}_2\text{NR}^4-$;

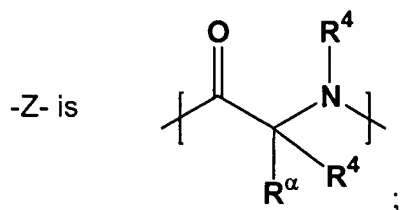
each W is independently selected from the group consisting of $-\text{NR}^4-$, $-\text{O}-$ and $-\text{S}-$;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of -Z- is S or R, or a mixture of S and R;

each R^a is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2-(2-imidazolyl)$, $-(CH_2)_4-NH_2$, $-(CH_2)_2-S-CH_3$, phenyl, CH_2 -phenyl, $-CH_2-OH$, $-CH(OH)-CH_3$, $-CH_2-(3-indolyl)$, $-CH_2-(4-hydroxyphenyl)$; and includes compounds wherein R^a and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, substituted $-(C_1-C_6)$ alkyl, $-(C_2-C_6)$ alkenyl, substituted $-(C_2-C_6)$ alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of $-R^4$, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NH)-NR^4_2$, $-(C_1-C_6)$ perfluoroalkyl, $-CF_2Cl$, $-P(=O)(OR^4)_2$, $-OP(=O)(OR^4)_2$, $-CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$; then R^4 is not -H;

each R^6 is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, and aryl(C_1-C_3)alkyl;

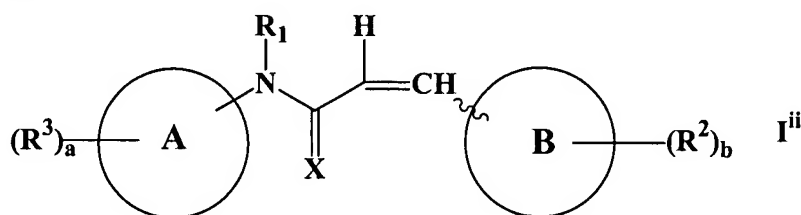
each R^7 is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, $-C(=O)R^8$, $-OR^4$, $-SR^4$, $-OC(=O)(CH_2)_2CO_2R^6$, guanidino, $-NR^4_2$, $-NR^4_3^+$, $-N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^a , halogen, $-NR^4_2$ and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within $[[Ar,]]$ R^1 , R^5 $[[R^6,]]$ R^7 and R^8 are independently selected from the group consisting of halogen, $-(C_1-C_6)alkyl$, $-(C_1-C_6)alkoxy$, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)alkyl$, $-OR^4$, $-(C_2-C_6)alkylene-OR^4$, phosphonato, $-NR^4_2$, $-NHC(=O)(C_1-C_6)alkyl$, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)alkyl$, $-O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)_2$ and $-(C_1-C_3)perfluoroalkyl$; or a salt of such a compound;

wherein the mitotic phase cell cycle inhibitor or topoisomerase inhibitor is other than a compound of formula Iⁱⁱ.

89. (currently amended) A method for treating cancer or other proliferative disorder comprising administering to an animal an effective amount at least one cytoprotective compound according to formula Iⁱⁱ:



wherein:

ring A and ring B are independently selected from the group consisting of aryl and heteroaryl;

X is O or S;

R^1 is independently selected from the group consisting of $-R^4$, $-SO_2(C_1-C_6)alkyl$, $-C(=O)R^4$, $-C(=O)OR^4$, $-C(=O)O(C_1-C_6)alkylenearyl$, $-OR^4$, $-(C_2-C_6)alkynyl$, $-(C_3-C_6)heteroalkenyl$, $-(C_2-C_6)alkylene-OR^4$, substituted aryl, unsubstituted aryl, substituted heteroaryl, unsubstituted heteroaryl, substituted aryl $(C_1-C_3)alkyl$, unsubstituted aryl $(C_1-C_3)alkyl$, substituted heteroaryl $(C_1-C_3)alkyl$ and unsubstituted heteroaryl $(C_1-C_3)alkyl$;

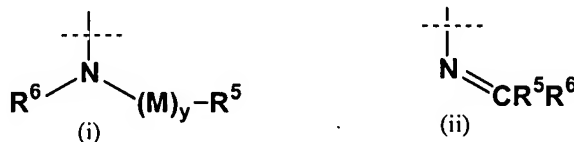
R^2 is independently selected from $-(C_1-C_6)alkyl$, halogen, $-OR^4$, $-C\equiv N$, $-NO_2$, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NR^4)NR^4_2$, $-O(C_1-C_3)alkylene-CO_2R^4$, $-(C_2-C_6)alkylene-OR^4$, phosphonato,

$-\text{NR}^4_2$, $-\text{NHC}(=\text{O})(\text{C}_1-\text{C}_6)\text{alkyl}$, sulfamyl, carbamyl, $-\text{OC}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$, $-\text{O}(\text{C}_2-\text{C}_6)\text{alkylene}-\text{N}((\text{C}_1-\text{C}_6)\text{alkyl})_2$, $-\text{S}(\text{C}_1-\text{C}_3)\text{alkyl}$, $-\text{S}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$, $-(\text{C}_1-\text{C}_3)\text{perfluoroalkyl}$ and $-\text{SO}_2(\text{C}_1-\text{C}_3)\text{alkyl}$;

b is 1, 2, 3, 4 or 5;

\sim indicates a single bond, whereby the compounds of formula I may be in either the E or the Z conformation;

R^3 is independently selected from halogen, $-(\text{C}_1-\text{C}_6)\text{alkyl}$, $-\text{OR}^4$, $-\text{C}\equiv\text{N}$, $-\text{C}(=\text{O})\text{NR}^4_2$, $-\text{C}(=\text{O})\text{OR}^4$, $-\text{C}(=\text{NR}^4)\text{NR}^4_2$, $-\text{O}(\text{C}_1-\text{C}_3)\text{alkylene}-\text{CO}_2\text{R}^4$, $-(\text{C}_1-\text{C}_6)\text{alkylene}-\text{OR}^4$, nitro, phosphonato, $-\text{NHC}(=\text{O})(\text{C}_1-\text{C}_6)\text{alkyl}$, sulfamyl, carbamyl, $-\text{OC}(=\text{O})(\text{C}_1-\text{C}_3)\text{alkyl}$, $-\text{O}(\text{C}_2-\text{C}_6)\text{alkylene}-\text{N}((\text{C}_1-\text{C}_6)\text{alkyl})_2$, $-(\text{C}_1-\text{C}_3)\text{perfluoroalkyl}$ and (i) and (ii) below:



wherein:

each M is a bivalent connecting group independently selected from the group consisting of $-(\text{C}_1-\text{C}_6)\text{alkylene}-$, $-(\text{CH}_2)_d-\text{V}-(\text{CH}_2)_e-$, $-(\text{CH}_2)_f-\text{W}-(\text{CH}_2)_g-$ and $-\text{Z}-$;

each y is independently selected from the group consisting of 0 and 1;

each V is independently selected from the group consisting of arylene, heteroarylene, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{O})(\text{C}_1-\text{C}_6)\text{perfluoroalkylene}-$, $-\text{C}(=\text{O})-$, $-\text{C}(=\text{S})-$, $-\text{S}(=\text{O})-$, $-\text{SO}_2-$, $-\text{C}(=\text{O})\text{NR}^4-$, $-\text{C}(=\text{S})\text{NR}^4-$ and $-\text{SO}_2\text{NR}^4-$;

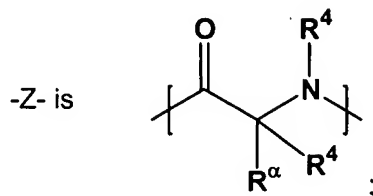
each W is independently selected from the group consisting of $-\text{NR}^4-$, $-\text{O}-$ and $-\text{S}-$;

each d is independently selected from the group consisting of 0, 1 and 2;

each e is independently selected from the group consisting of 0, 1 and 2;

each f is independently selected from the group consisting of 1, 2 and 3;

each g is independently selected from the group consisting of 0, 1 and 2;



wherein the absolute stereochemistry of -Z- is S or R, or a mixture of S and R;

each R^{α} is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, $-(CH_2)_3-NH-C(NH_2)(=NH)$, $-CH_2C(=O)NH_2$, $-CH_2COOH$, $-CH_2SH$, $-(CH_2)_2C(=O)-NH_2$, $-(CH_2)_2COOH$, $-CH_2-(2-imidazolyl)$, $-(CH_2)_4-NH_2$, $-(CH_2)_2-S-CH_3$, phenyl, CH_2 -phenyl, $-CH_2-OH$, $-CH(OH)-CH_3$, $-CH_2-(3-indolyl)$, $-CH_2-(4-hydroxyphenyl)$; and includes compounds wherein R^{α} and R^4 combine to form a 5-, 6- or 7-membered heterocyclic or carbocyclic ring;

a is 1, 2 or 3;

R^4 is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, substituted $-(C_1-C_6)$ alkyl, $-(C_2-C_6)$ alkenyl, substituted $-(C_2-C_6)$ alkenyl and heteroalkyl, wherein two R^4 groups may together form a heterocycle;

each R^5 is independently selected from the group consisting of $-R^4$, unsubstituted aryl, substituted aryl, substituted heterocyclic, unsubstituted heterocyclic, $-CO_2R^4$, $-C(=O)NR^4_2$, $-C(=NH)-NR^4_2$, $-(C_1-C_6)$ perfluoroalkyl, $-CF_2Cl$, $-P(=O)(OR^4)_2$, $-OP(=O)(OR^4)_2$, $-CR^4R^7R^8$ and a monovalent peptidyl moiety with a molecular weight of less than 1000; provided that when y is 0 and R^5 is $-CO_2R^4$; then R^4 is not -H;

each R^6 is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, and aryl(C_1-C_3)alkyl;

each R^7 is independently selected from the group consisting of -H, $-(C_1-C_6)$ alkyl, $-C(=O)R^8$, $-OR^4$, $-SR^4$, $-OC(=O)(CH_2)_2CO_2R^6$, guanidino, $-NR^4_2$, $-NR^4_3$, $-N^+(CH_2CH_2OR^5)_3$, halogen, phenyl, substituted phenyl, heterocyclyl, and substituted heterocyclyl; and

each R^8 is independently selected from the group consisting of R^{α} , halogen, $-NR^4_2$ and heterocycles containing two nitrogen atoms;

wherein the substituents for the substituted aryl and substituted heterocyclic groups comprising or included within $[[Ar,]]$ R^1 , R^5 $[[R^6,]]$ and R^7 and $-R^{\alpha}$ are

independently selected from the group consisting of halogen, $-(C_1-C_6)alkyl$, $-(C_1-C_6)alkoxy$, $-NO_2$, $-C\equiv N$, $-C(=O)O(C_1-C_3)alkyl$, $-OR^4$, $-(C_2-C_6)alkylene-OR^4$, phosphonato, $-NR^4_2$, $-NHC(=O)(C_1-C_6)alkyl$, sulfamyl, carbamyl, $-OC(=O)(C_1-C_3)alkyl$, $-O(C_2-C_6)alkylene-N((C_1-C_6)alkyl)_2$ and $-(C_1-C_3)perfluoroalkyl$; or a salt of such a compound;

followed by an effective amount of at least one mitotic phase cell cycle inhibitor or topoisomerase inhibitor after administration of the cytoprotective compound.

90. (new) A compound according to claim 1 wherein a is 2 or 3.

91. (new) A composition according to claim 35 wherein a is 2 or 3.